INDEX NUMBER

VOL. 32 DECEMBER, 1946 No. 6

AMERICAN HEART JOURNAL

For the Study of the

CIRCULATION

Published Monthly Under the Editorial Direction of The American Heart Association

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American Heart Journal

CONTENTS FOR DECEMBER, 1946

Vol. 32, No. 6, December, 1946, American Heart Journal is published monthly by The C. V. Mosby Company at Jefferson City, Mo. Editorial office: 3207 Washington Blvd., St. Louis 3, Mo. Subscription Price: United States, its Possessions, Pan-American Countries, $10.00; In Canada and other Foreign Countries, $11.00. Entered as Second-Class Matter at the Post Office at Jefferson City, Missouri, under the Act of March 3, 1879. Printed in the U. S. A.

American Heart Journal

VOL. 32 DECEMBER, 1946 NO. 6

THE EXPANDED PROGRAM OF THE AMERICAN HEART ASSOCIATION FOR 1947

NATIONAL HEART WEEK, FEBRUARY 9, 1947

THE current activities of the American Heart Association are of national interest to physicians as well as to laymen who have long looked for the development of a comprehensive public health program directed against diseases of the heart and blood vessels—the leading cause of death in the United States.

Those familiar with its growth will recall that the American Heart Association was founded in 1924 to combat the growing prevalence of heart disease. During the following two decades, the American Heart Association developed professional prestige and acceptance as the only national agency devoted to educational work relating to diseases of the heart. Organized primarily as a professional scientific organization, the Association concerned itself largely with the publication of the *American Heart Journal*, the only journal published in the United States which limits itself to problems of the heart and blood vessels; with the preparation of other materials for the postgraduate education of physicians; and with the establishment of standards in the field of cardiovascular disease.

The war stimulated the development of special activities particularly with reference to rheumatic fever. In 1944, recognizing the crucial need for a national program to fight rheumatic fever and rheumatic heart disease, the American Heart Association called a conference to consider the organization of a program. The conference was attended by representatives of practically all national voluntary health organizations and governmental agencies concerned with rheumatic fever and by representatives of the Army, Navy, U. S. Public Health Service, the Veteran's Administration, and the Children's Bureau.

Following this conference, the American Council on Rheumatic Fever of the American Heart Association was formed with representatives of twelve national medical agencies.* Today the Council is concerned with all phases of the American Heart Association's program which relate specifically to rheumatic fever. It operates administratively through the American Heart Association.

Earlier this year, the American Heart Association reorganized its administrative structure and broadened its objectives in order to meet the urgent need for national action in solving the medical, social, and economic problems of heart disease. Prominent laymen were admitted to membership on the various executive boards, and a program of interrelated membership with all local Heart Associations was instituted. In order to preserve the scientific aspects of the program of the American Heart Association, a Scientific Council, composed of representatives of all scientific fields contributing to our knowledge of heart disease, is being formed.

*American Academy of Pediatrics, American Association of Medical Social Workers, American College of Physicians, American Heart Association, Inc., American Hospital Association, American Medical Association, American Nurses' Association, American Public Health Association, American Rheumatism Association, American School Health Association, National Organization for Public Health Nursing, and National Society for Crippled Children and Adults.

The extent to which the American Heart Association has expanded its objectives is indicated in this condensed outline of its 1946-1947 program.† This program calls for the functioning of the American Heart Association as a clearing house for cardiovascular activities throughout the United States; for a national informational campaign to educate the public on essential problems of heart disease; for postgraduate education of the medical profession, including medical students, in cardiac and vascular diseases; for provision for the application of public health techniques to control rheumatic fever and other heart diseases through the establishment of standards for the many facilities needed in such programs, the stimulation of more accurate vital statistics, and the application of epidemiologic techniques to the study of heart disease and rheumatic fever; for the health education of other professional groups including social workers, teachers, school administrators, physical education instructors, school physicians, public health nurses, and public health workers; for aid to the cardiac patient in employment; for re-evaluation of cardiac disability in life, health, and accident insurance; and for sponsoring and financing clinical and laboratory research.

The recent award of $50,000 by the American Legion to the American Council on Rheumatic Fever of the American Heart Association has done much to initiate an important approach to rheumatic fever. One-half of this amount has been allotted to the creation of two three-year research fellowships. Twelve thousand five hundred dollars have gone to the establishment of a Statistician's Office which is providing a much-needed statistical service for planning community rheumatic fever registries and the preparation of satisfactory methods for the classification of deaths from heart diseases. The remainder of this grant is being spent for the first of a series of medical field consultants to work directly with communities requiring aid in setting up rheumatic fever programs.

The American Legion's grant illustrates the need of the American Heart Association and its affiliate, the American Council on Rheumatic Fever, for voluntary financial support in order to undertake the various activities outlined in its program. The 1947 budget of the Association requires a minimum of $286,000 for administration. Grants in aid for research projects call for an additional budget of $275,000. This total budget of $561,000, which has been approved by the National Budget Committee, represents the minimum goal required by the American Heart Association to carry forward its program and, at the same time, to create the basis for a national public fund-raising drive in 1948.

To provide the necessary public acceptance for such a drive, the American Heart Association is now conducting a nationwide program of public information and education on diseases of the heart and blood vessels. The public is being informed of the significance of high blood pressure, infections, overweight, rheumatic fever, and other factors contributing to various types of heart disease.

Plans have been developed for the observance of National Heart Week which is to be inaugurated Feb. 9, 1947. During this week, the importance of care, treatment, prevention, and study of circulatory problems will be emphasized, and the public will be reminded that heart disease is our *first* national health problem and that it can be combatted only with the fullest cooperation of the scientific worker, the specialist in heart and peripheral vascular diseases, the practicing physician, and the individual citizen and his community.

It is the plan of the American Heart Association to carry out selective fund-raising activities during National Heart Week and during the remainder of the year in cooperation with local Heart Associations where they exist. As the public becomes informed and aware of the significance of heart disease as a serious public health problem, the stage will be set for a comprehensive nationwide appeal for contributions in 1948.

†Those interested in securing a more detailed discussion of this program are requested to write to the American Heart Association, Inc., 1790 Broadway, New York, N. Y.

Original Communications

THE ESOPHAGEAL ELECTROCARDIOGRAM IN ARRHYTHMIAS AND TACHYCARDIAS

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THE technique of taking electrocardiographic tracings with an electrode in the esophagus is a procedure which dates from the early days of electrocardiographic research. Special studies[1-7] have demonstrated the use of these leads in a variety of conditions. The present paper deals only with the value of the esophageal electrocardiogram in certain arrhythmias and tachycardias, although it is also of recognized value in the study of the electrical field of the heart and in the diagnosis of posterior myocardial infarction.

There is nothing new or unique in this work, but for some time we have been impressed that certain electrocardiograms are difficult or impossible of accurate interpretation without absolute knowledge of the position of the P wave. All too often, both in published and unpublished reports, the interpretation has been based upon theory rather than on demonstrated fact, and it has seemed to us that in selected cases valuable additional information could be obtained by the use of the esophageal lead. For this reason, it has been our practice to take esophageal electrocardiograms in all cases where the P waves were not distinctly visible in any of the leads from the surface of the body. Occasionally the P waves may be augmented by paired leads from the right sternal border, but the most satisfactory lead for demonstration of P waves is derived from an electrode in the esophagus adjacent to the auricles. An electrode in this area produces a pattern approaching that obtained by a direct lead from the surface of the auricle.

Esophageal electrodes may be simple, having a single terminal at the tip of the tube, or they may be complex, having numerous terminals located at intervals near the tip. For all practical purposes, a single terminal is very satisfactory, and such a device may be constructed with a few minutes of labor. An ordinary Rehfuss stomach tube is cut to a length of about 70 centimeters. A small bolt which will conveniently fit the diameter of the tube is soldered to a fine copper wire (about No. 34). A globule of solder is attached to the head of the bolt to provide a round, smooth tip which acts as the contact with the wall of the esophagus. The wire is then inserted through the tube and connected to a terminal at the opposite end so that the wire is fairly taut in the tube. We have found that a terminal from the base of an old radio tube is very useful for this purpose. The tube is then marked in centimeters from the tip to the 55 cm.

From the Division of Cardiology, Department of Medicine, New York Post-Graduate Medical School and Hospital, Columbia University.
Received for publication April 30, 1946.

level with black lacquer. Care must be taken in cleaning the tube after use to avoid stretching the tube, for this may break the fine wire or one of the connections.

The technique of inserting the tube is exactly the same as for any stomach tube. We generally insert the tip through a nostril with the patient in the sitting position and push it into the esophagus during the act of deglutition as the patient drinks water. Most patients tolerate this procedure well and it is only occasionally necessary to anesthetize the pharynx. A small portion of electrode paste is rubbed on the tip just before insertion. After the tube is inserted to the 55 cm. level, the patient is placed in a supine position for the recording of the electrocardiogram. The esophageal lead can be paired with any other lead but we commonly use the left leg or preferably the indifferent electrode of Wilson.

Occasionally there is poor electrical contact with the esophagus after the tube is in place; this can often be improved by having the patient drink some warm saline solution. Another difficulty which produces artefacts in the record is sliding of the electrode on the mucous membrane of the esophagus with each beat of the heart. This produces very bizarre complexes but can usually be obviated by shifting the position of the electrode slightly.

At the 55 cm. level the tip of the tube is usually in the stomach. A record is taken at this level and the tube is then withdrawn in increments of 2.0 or 2.5 cm. to the 30 cm. level, which usually places the tip above the heart. Levels from 55 to 40 cm. are usually in close proximity to the diaphragmatic surface of the heart and accentuate the ventricular potentials, while those from the 40 to the 30 cm. levels usually overlie the auricles and accentuate the auricular potentials. At the lower levels one often encounters difficulty in keeping the string in the field due to respiratory movement of the diaphragm. This can usually be controlled by instructing the patient to suspend respiration temporarily at the end of a normal expiration. The amplifying types of electrocardiographic machines are somewhat easier to use in that the beam balances and stays in the field more easily, but all instruments are satisfactory and we have made many records on both string and amplifying instruments.

As a general rule, the following types of mechanisms offer difficulty in interpretation and may be inaccurately diagnosed due to inability to identify the P wave definitely:

1. Electrocardiograms in which the P wave is superimposed on the QRS complex or the T wave.
2. Electricardiograms in which the voltage of the P wave is too low to permit positive identification.
3. Tachycardia of either supraventricular or ventricular origin in which P waves cannot be definitely identified.

The following examples are presented to illustrate these points.

ILLUSTRATIVE ELECTROCARDIOGRAMS

The first case (Fig. 1) is an illustration of a P wave buried in the T wave. Esophageal leads are not usually necessary in this type of case for the P-R

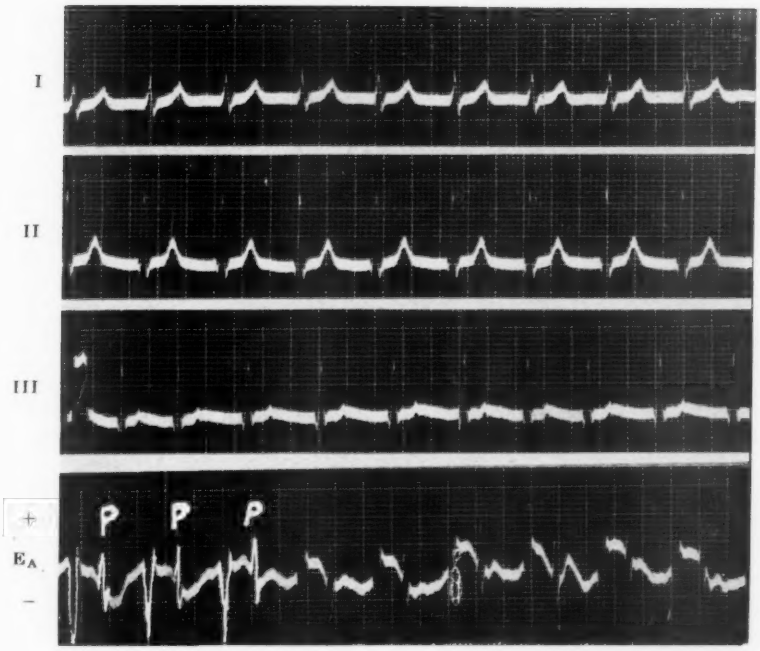

Fig. 1.—The standard leads in this case do not show definite P waves, but from the auricular level of the esophagus the P waves are seen to fall on the summit of the T waves. (The first three complexes of the lead from the auricular level of the esophasgus (E_A) have been retouched to improve reproduction, and the P waves are marked.)

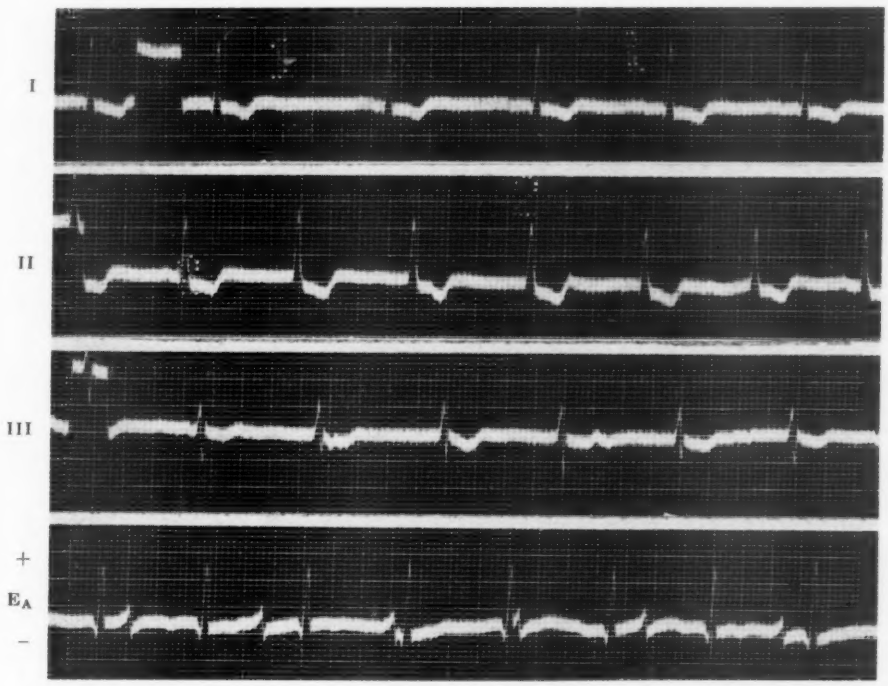

Fig. 2.—Electrocardiogram illustrating extremely low voltage of the P waves in the standard leads. The E_A lead clearly shows the P waves. There is complete dissociation between the auricles and ventricles.

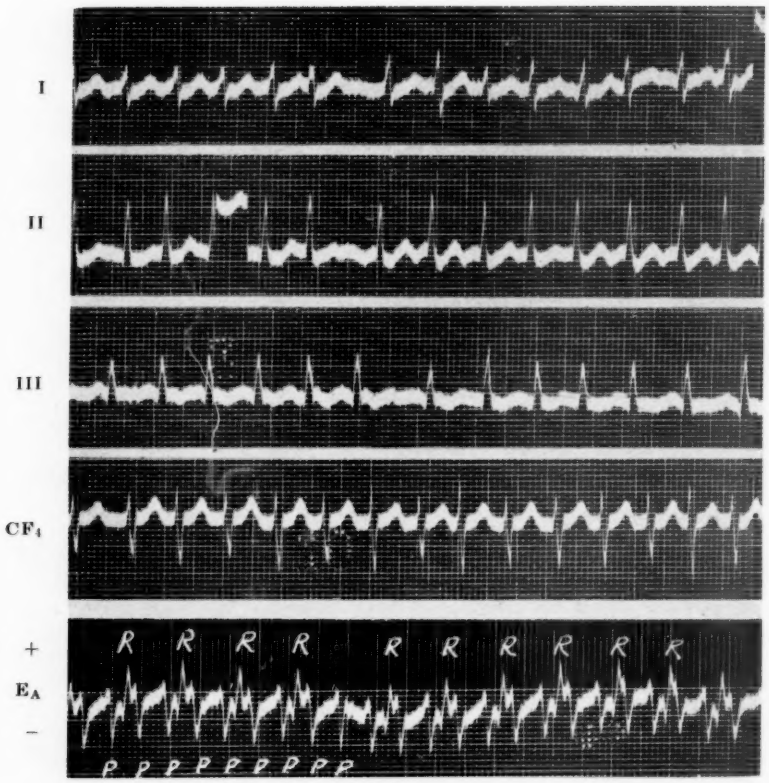

Fig. 3.

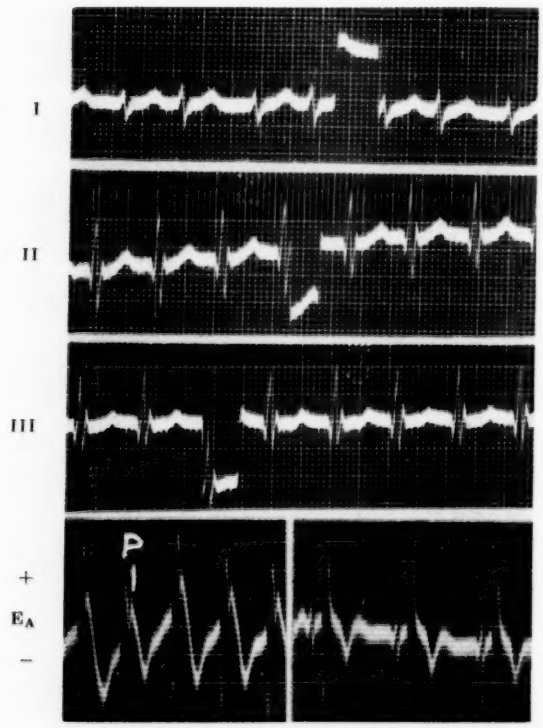

Fig. 4.

Fig. 3.— The standard leads reveal no definite P waves and an irregular rhythm. The supposition would be that one is dealing with rapid auricular fibrillation, although experienced electrocardiographers might suspect auricular flutter. The E_A lead clearly demonstrates that the mechanism is auricular flutter with varying block. The R waves are marked at the top and the P waves at the bottom of the E_A record.

Fig. 4.— No P waves are apparent in the standard leads, but the E_A lead shows a notching of the descending limb of S wave which represents the P wave. For comparison, a small portion of a tracing from the same level after return to normal rhythm is included. It can be seen that the P wave is now in its normal position in front of the QRS and the notching of the descending limb of the S wave has disappeared. This establishes a diagnosis of nodal tachycardia.

interval will vary from day to day, or accelerating the pulse by administration of atropine or by exercise will shift the P wave from the T wave so that it becomes visible. In this particular case the P-R interval returned to normal over a period of several weeks.

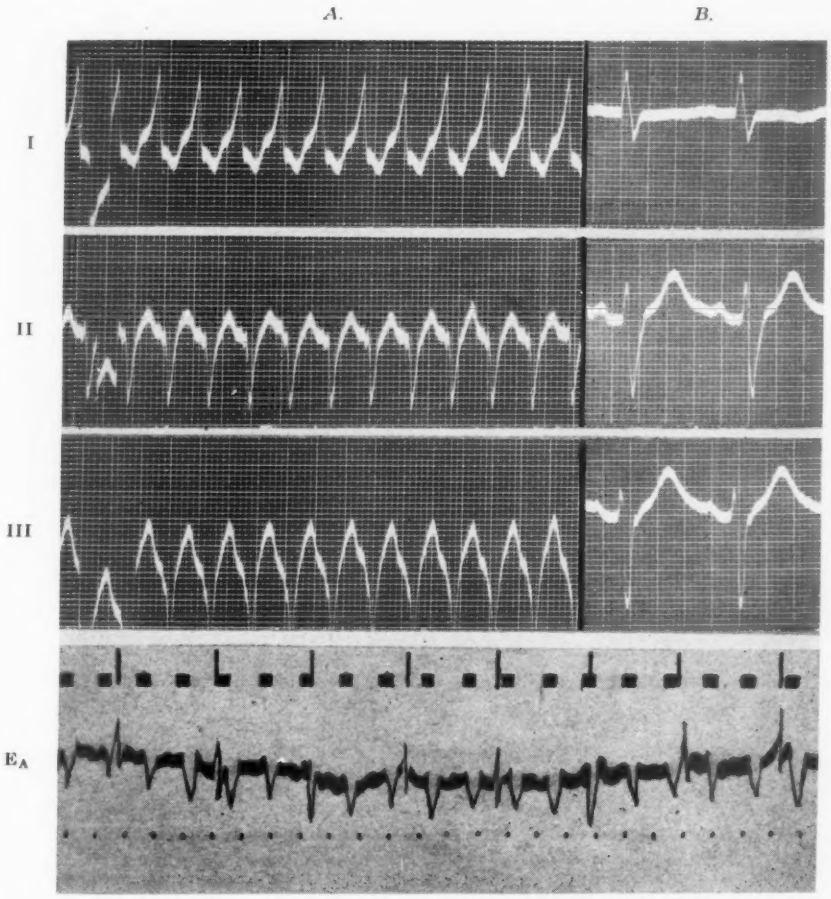

Fig. 5.—The leads under *B* show a marked ventricular conduction defect (RBBB) which was present prior to the tachycardia shown under *A*. Under these circumstances it seemed impossible to decide if this was a case of supraventricular tachycardia with a ventricular conduction defect or a ventricular tachycardia. The E_A lead definitely established the diagnosis of ventricular tachycardia. The small blocks at the top of the record represent the QRS complexes and the vertical lines, the P waves showing an independent auricular rhythm much slower than that of the ventricles. (The E_A lead is an exact tracing of the electrocardiogram and was made solely to improve reproduction.)

The electrocardiogram in Fig. 2 illustrates the type of case in which the voltage of the P wave is too low to make identification positive. There are suggestive P waves in Leads II and III, but they are not definite enough to be convincing. From the auricular level of the esophagus, however, the P waves stand out well and it is clearly seen that the auricles have an independent rhythm slower than that of the ventricles.

In Fig. 3 the rate is rapid and irregular, although there are sequences which seem fairly regular. No definite P waves can be identified, and the most obvious diagnosis would be rapid auricular fibrillation although experienced electrocardiographers would suspect flutter. The esophageal lead at the auricular level (E_A) reveals definite flutter waves which are perfectly regular at a rate of 300 per minute in contrast to the ventricular rate of about 140.

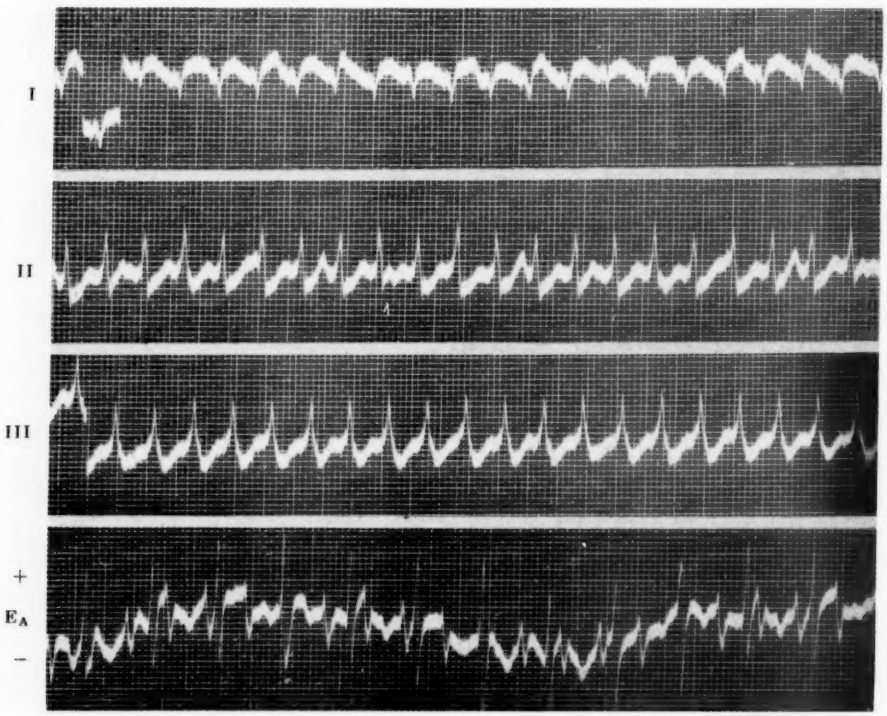

Fig. 6.—This is the electrocardiogram of a 44-year-old man during an episode of tachycardia which occurred one week after an acute anterior myocardial infarction. The esophageal electrocardiogram shows very large P waves at a slower rhythm than that of the ventricles.

Fig. 4 illustrates a case of paroxysmal tachycardia which was assumed to be nodal rhythm because no P waves could be identified in the standard leads. The esophageal lead revealed the P wave on the descending limb of the S wave. A tracing from the same level after return to normal sinus rhythm is also included and the P waves are clearly present before each QRS complex, and the notching on the downstroke of the S wave has disappeared although the remainder of the QRS and the T waves have not been altered. This proves the original assumption of nodal rhythm.

Fig. 5 shows electrocardiograms of a 52-year-old man who was subject to frequent attacks of paroxysmal tachycardia. It is of interest that electrocardiograms taken during periods of normal rhythm (*B*) revealed a marked intra-

ventricular conduction disturbance. When we succeeded in obtaining a record during an episode of tachycardia (*A*), it had the appearance of a ventricular tachycardia, but because of the previous conduction disturbance, it was not clear whether this was a true ventricular tachycardia or a supraventricular tachycardia in the presence of the previously demonstrated ventricular conduction disturbance. An esophageal electrocardiogram was therefore recorded, an actual tracing of which is shown at the bottom of Fig. 5. (A tracing is used rather than the original record solely to improve reproduction.) The small blocks at the top of the tracing represent QRS complexes and the vertical lines represent P waves. This record clearly shows a slow auricular rate independent of the ventricular rate and establishes the diagnosis of ventricular tachycardia.

The last illustration (Fig. 6) shows the electrocardiogram taken on a 44-year-old man during an episode of sudden tachycardia which occurred one week after an acute anterior myocardial infarction. The standard leads were not considered sufficiently diagnostic to differentiate between auricular tachycardia, nodal tachycardia, auricular flutter, and ventricular tachycardia, so an esophageal electrocardiogram was taken. This procedure did not upset the patient in any way. The E_A lead shows very large P waves which overshadow the QRS complexes. These waves were at a slower rate and independent of the ventricular complexes, showing that the origin of the tachycardia was below the auricles. The patient was treated with large doses of quinidine sulfate by mouth and the abnormal rhythm was converted to a normal sinus rhythm within a few hours. Further convalescence was uneventful. Leads from the ventricular level of the esophagus (not illustrated) revealed a characteristic depression of the S-T segments which is commonly seen with anterior myocardial infarction.

DISCUSSION

Our purpose in presenting this material is to emphasize the value of the esophageal electrocardiogram in making accurate diagnosis in certain cases of tachycardia and arrhythmia. We feel this procedure has, in general, been neglected. The records are easy to take and simple to interpret after a short period of orientation.

Accurate interpretation is important not only to further our knowledge of electrocardiography and to prevent inaccurate diagnosis from infiltrating the literature, but also because of the necessity of having an accurate diagnosis on which to base proper therapy.

SUMMARY

1. Several electrocardiograms are reproduced, illustrating the value of the esophageal electrocardiogram in accurately diagnosing certain types of arrhythmia and tachycardia.

2. A plea has been made for more frequent use of the esophageal electrocardiogram in selected cases.

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ANOXEMIA AND EXERCISE TESTS IN THE DIAGNOSIS OF CORONARY DISEASE

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SINCE the usefulness of functional tests in the diagnosis of coronary heart disease still seems to be under discussion, this paper attempts to answer some of the questions pertaining to this matter from a clinical point of view.

According to Blumgart and co-workers,[1] coronary heart disease comprises angina pectoris, coronary failure, and acute myocardial infarction. In the last two conditions the patient is seriously ill and no consideration will be given to the aid that functional tests afford in making the diagnosis. The application of improved diagnostic measures will be limited to angina pectoris. Does the clinical management of angina pectoris require methods of study other than the history, physical examination, electrocardiogram, roentgenogram, and ordinary laboratory tests? Some experienced clinicians perhaps would answer in the negative. They feel sure that the diagnosis is best made from the history and usual clinical examination. Others feel a need for more objective methods in dealing with a condition which is subjective in its manifestations.

White[2] has stated that 25 per cent of his patients with a history of angina do not show any abnormality of the heart by the usual methods of examination. In about 150 of our patients with suspected angina (perhaps a somewhat less well-defined group than White's) the diagnosis of this condition was reasonably certain in only one-sixth; of the others, coronary artery disease was strongly suspected in two-thirds, and in one-sixth the diagnosis was in doubt. With the increasing incidence of cardiac neuroses, social and military benefits, and, perhaps, compulsory health insurance, the needs for improved objective diagnostic measures are definite. For experimental purposes and for studies before and after surgical procedures on the heart they are also useful beyond question.

For which types of patients are tests especially desirable? There are three groups to be dealt with: (1) patients with some sort of disorder in the chest, very slightly suggestive of angina; (2) patients whose symptoms resemble those of angina, but whose chest pain is mild or otherwise atypical; and (3) patients with clear-cut angina, with or without previous myocardial infarction.

The main purpose of "coronary" tests is to reveal a latent coronary insufficiency. This means that tests are indicated in suspected cases without a "coronary" electrocardiogram at rest. It is also likely that additional strain brought about by tests, even in patients with a coronary electrocardiogram at rest, will give some evidence of the remaining so-called "coronary reserve."

Even if one admits that in the first group of patients with slightly suspected angina the use of "coronary" tests can be confined to those in whom no other

From the Sabbatsberg's Hospital.
Read before the Harvard Medical Society, Boston, Feb. 12, 1946.
Received for publication May 9, 1945.

positive diagnosis could be obtained and, also, that in the third group, the members of which give a very convincing history of angina and usually some positive findings on clinical examination, the use of the tests is of limited value, there still remains the large second group of patients with moderately suspected angina, many of whom will not show evidence of coronary insufficiency in the electrocardiogram at rest. This is the group in which tests, from a diagnostic standpoint, are most desirable. With regard to the determination of the "coronary reserve" in patients with a coronary electrocardiogram at rest, it is too early to evaluate its prognostic significance. Sufficient statistics are as yet not available. As long as that problem is not solved, it is reasonable to continue to perform the tests also in this group of patients for later follow-up studies.

Assuming that tests are desirable, how should they be planned? Anginal pain and its equivalents are supposed to represent, clinically, a local ischemia of the myocardium, as do the electrocardiographic findings usually mentioned as evidence of coronary insufficiency. The test should, therefore, provoke pathologic changes in the coronary circulation and cause a relative disproportion between the demands of the myocardium for oxygenation and the supply of oxyhemoglobin through the coronary blood flow, thus eliciting either anginal pain or typical electrocardiographic changes, or both.

There are at least three ways to provoke such conditions and responses. One can reduce the oxygen saturation of the blood, either by giving a patient a gas mixture which is deficient in oxygen or by using a low-pressure chamber; one can exercise the patient, which increases the cardiac demand for oxygen without reducing the supply; or one can increase the work of the heart by adrenalin, which is a very dangerous method that we have not used. Apart from other considerations, the first method, the anoxemia test, is probably to be preferred for the study of the coronary circulation per se, and the second one, the exercise test, for the estimation of its capacity in the more natural environment of the whole system of reflexes, body metabolism, and hormonal activity

In the anoxemia test (in Sweden we prefer to call it the hypoxemia test) we use, according to the technique devised by Levy and associates,[3] 10 per cent oxygen and 90 per cent nitrogen breathed for twenty minutes, or less in case definite anginal pain or other unpleasant reactions should develop. Immediately after finishing the test, the patient is allowed to breathe 100 per cent oxygen for at least five minutes. We have also felt it wise, for the sake of comparison, to use the original criteria of Levy and co-workers[3b] in the interpretation of the electrocardiographic findings (Table I). In a later paper[3d] they discarded their fourth criterion.

There are at least two remarks to be made about the discrepancy between the theory and the reality of this test. The first concerns the oxygen saturation of the blood. Because of different types of breathing during the period of anoxemia, even in case of good pulmonary function, the oxygen saturation of the arterial blood, and probably also the carbon dioxide content and the pH of the blood, will differ from patient to patient. The same oxygen percentage in the inspired air will mean, to some extent, different things to different patients.

TABLE I. CRITERIA

Anoxemia.—The test is positive if any one of the following is found:

1. The arithmetic sum of the S-T deviations in Leads I, II, III, and IV F is greater by 3 mm. or more than in the control.
2. There is partial or complete reversal of the direction of the T wave in Lead I, accompanied by an S-T deviation of 1 mm. or more in this lead.
3. There is complete reversal of the direction of the T wave in Lead IV F, regardless of any S-T deviation in this lead.
4. There is partial reversal of the direction of the T wave in Lead IV F, accompanied by an S-T deviation of 1 mm. or more in this lead.

Exercise (New, "rigid" set of criteria)*.—The test is positive if:

1. The S-T depressions in Leads I, II, and III exceed together 2 mm.
2. T_1 or T_2 are inverted.
3. T_1 is diphasic and S-T_1 is depressed at least 1 mm.
4. Any single S-T depression is 1.5 mm. or more.

*These are to be regarded only as an attempt to establish better criteria than we formerly had. They may be changed following further experience and later follow-up studies.

Perhaps this objection can be met by using the Millikan oximeter for serial readings. If it works well, it is possible that the test, in the future, can be standardized according to the oxygen saturation of the blood rather than by the oxygen percentage in the inspired air.

The other objection to be discussed concerns the interpretation of the so-called coronary changes that appear in the electrocardiogram. There is still (perhaps now more than at any time) much obscurity about the underlying mechanism both with regard to the production of pain and with regard to the electrocardiographic signs of coronary insufficiency. The number of causal explanations is still increasing, and the importance of functional influences is more and more stressed. Such criticism is correct. It is obvious that further electrocardiographic, biochemical, and physiologic studies are greatly needed. But, in my opinion, this criticism should not retard attempts to gain further information about the reactions of the heart with diseased coronary arteries. It may, however, dispose us to a certain caution in our interpretation of the tests.

With this in mind, how does the anoxemia test work out clinically? In Table II are shown the results with anoxemia tests which have been published by Larsen (1938),[4] by Levy and associates (1941) [3b, 3c] and by Pruitt, Burchell, and Barnes (1945),[5] together with our own material which has been collected since 1942, when the test was introduced in Sweden by Dr. Gustav Nylin. In 1944, I had the opportunity to make the first survey of the test's results.[6] The report of Burnett, Nims, and Josephson[7] is not included since the use of a different oxygen tension of gas mixture prevents a comparison of their results with ours.

Table II is made up with regard to the previously mentioned three groups of patients with suspected angina, and the published statistics are classified according to these groups. Contrary to the procedure of the others, my clinical classification has been made without knowing the form of the electrocardiogram at rest.

TABLE II. COMPARISON BETWEEN PERCENTAGE OF POSITIVE ANOXEMIA TESTS IN THREE MAIN CLINICAL GROUPS, COMPILED FROM REPORTS OF VARIOUS INVESTIGATORS

INVESTIGATOR	GROUP I NORMALS AND SLIGHTLY SUSPECTED "CORONARY" CASES		GROUP II MODERATELY SUSPECTED "CORONARY" CASES		GROUP III PROBABLE OR CERTAIN "CORONARY" CASES	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Larsen (1938)[4] (9% O_2)	28	0	26	15	17	77
Levy (1941)[3b]	115	0	33	18	22 73	31* 55†
Pruitt, Burchell, and Barnes (1945)[5]	89	1.1	108	19.5	92	53
Biörck (1946)[6]	149	2.7‡	131	19.8	46 20	30 40§

*No anginal pain.
†Anginal pain.
‡Four positive tests in cases with definite pulmonary disease or other types of heart disease but no "coronary" symptoms.
§Abnormal ECG at rest.

There seem to be four conclusions to be drawn from Table II: (1) There are no positive tests in the group of normal subjects or patients with slightly suspected angina, if evidence of other cardiac disease, definite respiratory impairment, or severe anemia is ruled out. (2) One will have to expect about 20 per cent positive tests in the moderately suspected group. This figure is surprisingly constant throughout the three series of statistics which are based upon identical technique and criteria. In my material the figure is 18 per cent in 100 patients without a coronary electrocardiogram at rest, and 27 per cent in thirty-one with a coronary electrocardiogram at rest; in the whole group, it is 19.8 per cent. (3) Between 30 and 50 per cent of the patients with probable or certain coronary disease will show a positive test. (4) The conclusion follows that a negative test does not exclude the existence of coronary disease. Since Table II is based upon a study of 939 cases it should have statistical significance.

What is the correlation between the outcome of the test and the findings at autopsy? Although functional influences may be of some importance in the production of the anginal syndrome, we must, for the verification of our diagnosis, rely on the anatomic findings. Table III shows a comparison between the results of the anoxemia tests and the post-mortem findings, or, when no post-mortem study was performed, the type of death: an acute death, which probably resulted from myocardial infarction, ventricular fibrillation, or asystole; or, in contrast, death from progressive congestive failure or from intercurrent disease. The figures are collected from Levy's publications and from our material. The series thus studied is not as yet very large, but the results are rather striking.

TABLE III. CORRELATION BETWEEN RESULTS OF ANOXEMIA TESTS AND CONDITION OF CORONARY VESSELS AT AUTOPSY OR TYPE OF DEATH

	POST-MORTEM FINDINGS				NO POST-MORTEM TYPE OF DEATH			
	MARKED CORONARY SCLEROSIS		SLIGHT OR NO CORONARY SCLEROSIS		ACUTE DEATH		CONGESTIVE FAILURE	
	LEVY[3c]	BIÖRCK[6]	LEVY[3c]	BIÖRCK[6]	LEVY[3c]	BIÖRCK[6]	LEVY[3c]	BIÖRCK[6]
Positive tests	1	1	—	—	5	1	—	—
Negative tests								
Abnormal ECG at rest	2	2	—	—	1	2	3	—
Normal ECG at rest	—	—	1	2		—		2
Negative tests with anginal pain					4	1?		

It will be of great interest to follow up a larger autopsy series. For our part, we have also separated a group of "doubtful" cases, with electrocardiograms definitely changed, but not sufficiently so to fit in with Levy's rather rigid criteria; we intend to follow this group also in order to estimate the significance of such slighter changes.

It is the general experience that in some cases the test can change from positive to negative after an interval of time has elapsed. This may be ascribed, in part, to so-called functional influences, but it may also be the expression of substantial changes in the coronary circulation. The development of coronary sclerosis is not a constantly progressive process but one which occurs stepwise. A sudden narrowing or occlusion may produce a state of impending infarction, accidentally disclosed by a test; at the time of the next test a sufficient collateral circulation may have been established to result in a negative test. It is possible that a stable positive test is a more favorable sign than a changing one, for the latter may indicate either an active sclerotic process or a functional instability, both equally undesirable.

In this connection it is proper to discuss the hazard of the test. Table IV shows the unpleasant reactions which have been reported. In addition to these figures, there may be mentioned two other cases of pulmonary edema in Levy's earliest cases, and two vasovagal reactions which occurred in our clinic in 1945. The vasovagal reactions are probably partly unavoidable; they are usually not accompanied by coronary tracings, and they are, with proper observation and treatment, harmless. Psychogenic reactions are likewise hard to avoid because some of these cases cannot be valuated without the test. If the test is performed on proper indications, if the technique is well controlled, and if the observation of the patient is careful, trouble should not occur.

TABLE IV. UNPLEASANT REACTIONS DURING ANOXEMIA TEST

	LEVY[3b]	LEVY[3c]	PRUITT, BURCHELL, AND BARNES[5]	BIÖRCK[6]
Total number of patients	262	137	289	326
Reactions				
Vasovagal syncope	12 (11)*	8 (6)	9	1
Unconsciousness		2 (1)	3	
Convulsions	1			
Cardiac arrhythmia			3	?
Pulmonary edema		1		
Severe anxiety; hysteria	1	5 (3)	1	1

*Figures in brackets indicate number of patients with that reaction.

In some cases the test brings about severe anginal pain without marked changes in the electrocardiogram at the time it is interrupted. If there is real anginal pain, which is, in some cases, hard to judge objectively, Levy's and also our experience is that coronary disease is very probable. It is possible that an ischemic area, not located near either the endocardium or the epicardium, can be responsible for this circumstance. It is also possible that cardiac pain can arise in the walls of the coronary vessels. As the anoxemia test, as well as other tests, should be regarded only as an aid to the clinical diagnosis, we probably still should limit the criteria of a positive test to objective findings, although we may feel quite free to evaluate the provocation of pain for what it may be worth in our clinical conception of the patients' state.

Finally, a few words about exercise tests. In the United States these tests have been studied and used by Master[8] and Riseman and co-workers.[9] These investigators have used a two-step test; Master has used standardized work while Riseman and co-workers have continued exercise until pain appeared. In performing the exercise test, we have used Nylin's staircase, which is also used for functional studies of the oxygen consumption. The work is generally standardized to 5 rounds at a rate of 160 steps per minute, which most patients whom we expose to this test are able to perform without pathologic increase of their oxygen debt. Our opinion is that exercise tests should be standardized if the results are to be judged by the electrocardiograms. If the patients are allowed to work until they experience pain (which is a subjective limit), it is more logical to judge results from the amount of work performed rather than from changes in the electrocardiograms. The time between the completion of the work and the taking of the electrocardiograms is of importance. We have had the privilege of working with Elmqvist's electrocardiographic instrument, which simultaneously records five leads on the same piece of photographic paper.

Because of the differences in technique, it is hard to compare our results with those obtained by American workers. There is also the question of criteria. None of those who have written on exercise tests has used the same criteria. It is our experience that, in the case of exercise tests, much of their usefulness depends

upon the criteria applied. Formerly, we used very liberal criteria for positive tests. Since we found that about 25 per cent of the positive tests were obtained in those in whom coronary artery disease was not suspected (Group I of Table V), we now apply more rigid criteria which are very similar to those employed in the anoxemia test. Table V shows a comparison, in a series of 178 patients, of the results of the anoxemia test with those of the exercise test, the latter judged by means of both our old and our new criteria. Of 178 patients tested, 154 gave a negative result with both tests. In twenty-nine, the anoxemia tests showed a greater number of positive results than did the exercise test; in fourteen, the exercise test gave the greater number of positive results. The conclusion, therefore, seems justified that these tests should be used side by side in order to give a more comprehensive view of the condition. Having used both tests, we are of the opinion that they are about equally safe in the average patient, that the exercise test is perhaps a little simpler to perform, and that the anoxemia test probably gives more useful information than does the exercise test. Master and associates[10] have recently compared the effects of their two-step test with the effects of the anoxemia test, done by the Levy method, in 117 persons. They found that both tests gave similar results. They have, however, regarded the exercise test as positive if any S-T segment was deviated more than 0.5 mm. or if the T wave became inverted in any lead. These criteria are, in our experience, far too liberal. The question is, after all, not to obtain the largest possible number of positive tests but to obtain positive tests which, with certainty, correspond to the physiopathologic condition for which the test is intended.

TABLE V. COMPARISON BETWEEN ANOXEMIA AND EXERCISE TESTS

GROUP	ANOXEMIA		EXERCISE			
			OLD CRITERIA		NEW CRITERIA	
	POSITIVE	DOUBTFUL	POSITIVE	DOUBTFUL	POSITIVE	DOUBTFUL
I. Without suspected coronary disease	1	4	6	5	2	4
II. With suspected coronary disease	11	7	12	2	7	3
III. With probable or certain coronary disease	7	7	6	3	5	1
	19	18	24	10	14	8
	37		34		22	

As a general conclusion concerning the usefulness of these tests, the following may be said. Because they require technical equipment, a careful general examination of the patient with regard to indications and contraindications, and a certain experience with regard to their interpretation, and also because they

involve a slight chance of unpleasant and perhaps alarming reactions, they are not to be recommended for general use. Where possible, it is preferable to refer candidates for the test to a special heart service. In heart clinics and laboratories where experimental studies concerning "coronary" problems are carried out, these tests should be used. The first series of cases may be disappointing; that was our first impression. But only sufficient statistics can give the proper answer.

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PLASMA CONCENTRATIONS OF QUINIDINE WITH PARTICULAR REFERENCE TO THERAPEUTICALLY EFFECTIVE LEVELS IN TWO CASES OF PAROXYSMAL NODAL TACHYCARDIA

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IN THE past, methods for the estimation of cinchona alkaloids in biologic fluids and tissue were technically difficult and relatively insensitive.[1-3] Recently, however, Brodie and co-workers have reported new methods, based on colorimetry, which obviate these objections.[4-6]

The purpose of this paper is to report (1) plasma concentrations of quinidine in nineteen patients after a single oral dose of 1.0 Gm. of quinidine sulfate and (2) the therapeutic range of plasma concentration of quinidine in two cases of paroxysmal nodal tachycardia.

METHODS

The colorimetric method developed by Brodie[6] was used for the estimation of plasma quinidine concentrations in this study. This method involves the extraction of the alkaloid from alkalinized plasma by means of ethylene dichloride. Acid degeneration products, presumably phenolic in character, are then removed from the organic phase by means of an alkalinized alcoholic wash. Next the ethylene dichloride and contained alkaloid are shaken with methyl orange. The result of this step is the formation of a colored compound of the alkaloid and the dye. Measurement of the optical density of this compound is then made in the Evelyn photoelectric colorimeter against suitably prepared standards. With each set of plasma determinations, one or more recoveries were run, of which the majority fell within 90 to 100 per cent.

Nineteen adult patients (nine men and ten women, whose ages ranged from 20 to 60 years) were given a single dose of 1.0 Gm. of quinidine sulfate orally. These patients were selected so as to exclude obvious gastrointestinal, liver, and renal disease, thus minimizing possible interference with the normal processes of absorption, localization, degradation, and excretion of the alkaloid. All of the patients were confined to bed during the test. Sixteen of them ate regular meals. Of these, the majority received the 1.0 Gm. dose one to one and one-half hours before breakfast, while the others received the quinidine several hours after breakfast or after the noon meal. The remaining three patients of the nineteen were fasting for the eight hours preceding and the eight hours following the drug.

Blood specimens were collected in most instances every fifteen minutes for the first hour after the oral dose of the drug, and then at two, three, four, six,

Received for publication April 29, 1946.
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and eight hours. Ten patients also had levels taken at ten and twelve hours, and six at twenty-four hours.

The dose of 1.0 Gm. of quinidine sulfate was decided upon because of the possibility of inaccuracy with the colorimetric method at plasma quinidine concentrations much lower than those afforded by this quantity. In order to insure accurate dosage, the contents of each capsule of the drug had been carefully weighed.

Two ambulatory patients with paroxysmal nodal tachycardia were also studied over a period of four and one-half months, during which time observations were made on the relationship between varying plasma concentrations and therapeutic effect. A therapeutic regime was established for both patients in which a fixed dose of quinidine sulfate was given at four-hour intervals, day and night, for periods of from three to four weeks, during which periods stabilized plasma levels were obtained. The dose of the drug was progressively reduced by 25 per cent with each successive period. Blood samples were drawn from four to twelve times a week, usually three hours after the nearest dose. An inquiry into any symptoms and a recording of the pulse were made at each bleeding. Occasionally the effect of exercise upon the pulse rate was also recorded. Electrocardiograms were taken whenever an attack of tachycardia occurred and following reconversion to regular sinus rhythm.

RESULTS

1. Plasma Concentrations Attained in Nineteen Patients After a Single Oral Dose of Quinidine Sulfate.—Table I and Figs. 1 and 2 show the relationship of plasma concentration to time after a single oral dose of 1.0 Gm. of quinidine sulfate. The patients on whom data are given in Fig. 1 had the eight-hour

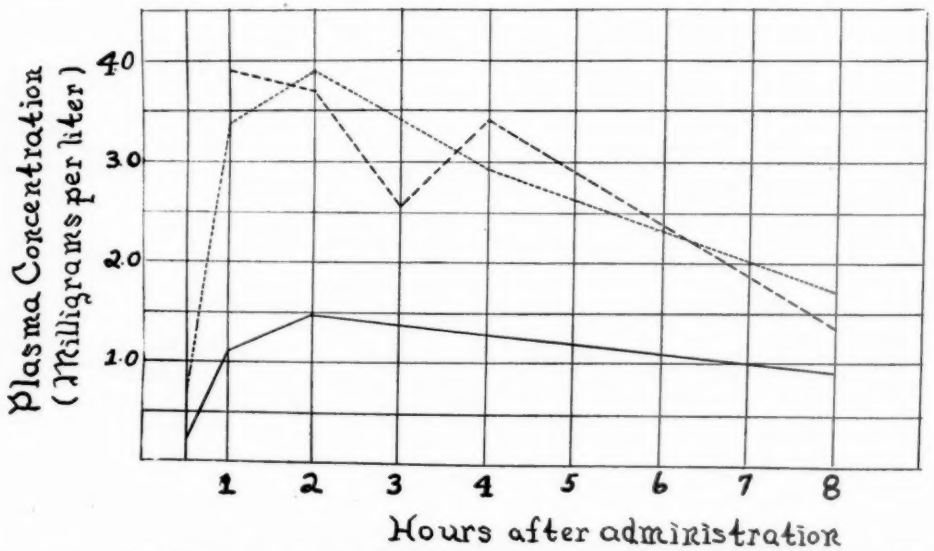

Fig. 1.—Quinidine plasma concentration curves in three patients given 1.0 Gm. of quinidine sulfate as a single oral dose. (Fasting subjects.)

TABLE I. SUMMARY OF PERTINENT DATA ON EACH OF TWENTY PATIENTS GIVEN 1.0 GM OF QUINIDINE SULFATE ORALLY

PATIENT	1	2	3	4	5	6	7	8	9	10
SEX	M	M	M	F	M	F	F	F	F	F
HEIGHT	5′ 9½″	5′ 4″	5′ 4″		5′ 4″	5′ 3″	5′ 5″	5′ 5″	5′ 1″	5′ 1″
WEIGHT	151	143	137		185	135	112	132	106	101
Quinidine blood levels (mg./liter plasma)										
15 min.	0.00	0.48	0.12	0.12	0.00	0.28	0.20	0.00	1.28	0.00
30 min.	0.20	2.88	1.44	0.00	0.00	1.68	0.60	0.00	2.68	1.68
45 min.	0.48	2.08	1.96	0.40	0.24	1.50	0.88	0.12	3.66	2.88
1 hr.	0.52	2.28	2.04	0.70	0.68	1.84	1.52	0.28	3.72	2.88
2 hr.	2.04	3.36	2.12	2.76	0.92	2.00	3.52	1.28	2.88	3.64
3 hr.	2.08	3.12	2.04	2.84	1.52	1.80	3.48	2.28	2.24	3.84
4 hr.	2.04	2.48	1.80	3.40	1.72	1.80	2.76	2.40	1.92	2.92
6 hr.	2.00	1.92	1.68	3.00	1.08	1.52	2.04	2.04	1.40	2.08
8 hr.	1.90	1.32	1.08	2.12	0.72	1.12	1.68	1.32	0.92	1.16
10 hr.			0.72				1.04	0.92	0.48	0.84
12 hr.			0.42				0.88	0.72	0.36	0.44
24 hr.			0.16						0.28	0.00
Maximum level	2.08	3.36	2.12	3.40	1.72	2.00	3.52	2.40	3.72	3.84
Time of maximum level	3 hr.	2 hr.	2 hr.	4 hr.	4 hr.	2 hr.	2 hr.	4 hr.	1 hr.	3 hr.
Percentage loss in plasma concentration from time of dose										
6 hr.	4%	43%	21%	12%	37%	24%	42%	15%	62%	46%
8 hr.	9%	60%	50%	37%	60%	44%	52%	45%	75%	70%
12 hr.			80%				75%	70%	87%	90%
24 hr.			92%						92%	100%
Patient	1	2	3	4	5	6	7	8	9	10

PATIENT	11	12	13	14	15	16	17	18	19	20
SEX	F	M	M	F	M	M	F	M	F	F
HEIGHT	5′ 5″	5′ 9″	5′ 3″	5′ 3″	5′ 11″		5′ 2″½	5′ 8″	5′ 0″	5′ 1″
WEIGHT	119	172	146	99	140		111	129	114	92
Quinidine blood levels (mg./liter plasma)										
15 min.	0.36			0.20	0.00	0.48				
30 min.	0.96	0.00	0.40	0.96	0.76	1.40	0.44	0.20	0.72	
45 min.	1.56	1.20	0.88	1.32	2.56	1.80	1.24			
1 hr.	1.40	1.56	1.40	1.52	2.56	2.92	1.72	1.12	3.36	3.88
2 hr.	2.04	2.56	2.72	2.84	2.08		4.32	1.48	3.88	3.72
3 hr.	2.56	2.88	2.44	2.48	2.40		4.32	1.40		2.56
4 hr.	2.44	2.48	2.20	2.12	1.68		3.72	1.36	2.96	3.44
6 hr.	1.68	2.08	1.68	1.72	1.32		2.84			
8 hr.	1.20	1.40	1.32	1.28	0.72		2.79	0.88	1.72	1.36
10 hr.	0.64	1.12	1.20	0.76	0.60					
12 hr.	0.32	1.16	0.92	0.44	0.12		1.76			
24 hr.	0.00			0.24	0.00					
Maximum level	2.56	2.88	2.72	2.84	2.56		4.32	1.48	3.88	3.88
Time of maximum level	3 hr.	3 hr.	2 hr.	2 hr.	¾ hr.		3 hr.	2 hr.	2 hr.	1 hr.
Percentage loss in plasma concentration from time of dose										
6 hr.	34%	28%	40%	40%	48%		34%			
8 hr.	53%	51%	51%	55%	71%		47%	40%	56%	65%
12 hr.	88%	60%	66%	84%	95%		75%			
24 hr.	100%			92%	100%		96%			
Patient	11	12	13	14	15	16	17	18	19	20

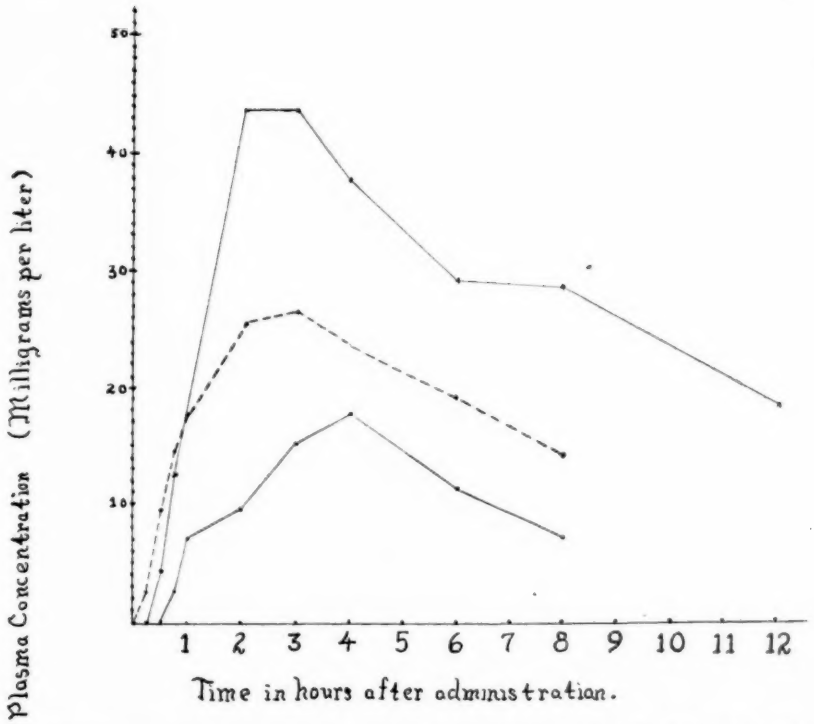

Fig. 2.—The middle curve represents the average concentration at each time period of the sixteen nonfasting patients. The upper curve is that of the patient who attained the highest plasma concentration among the sixteen patients. The lower curve is that of the patient who attained the minimum plasma concentration among the sixteen patients.

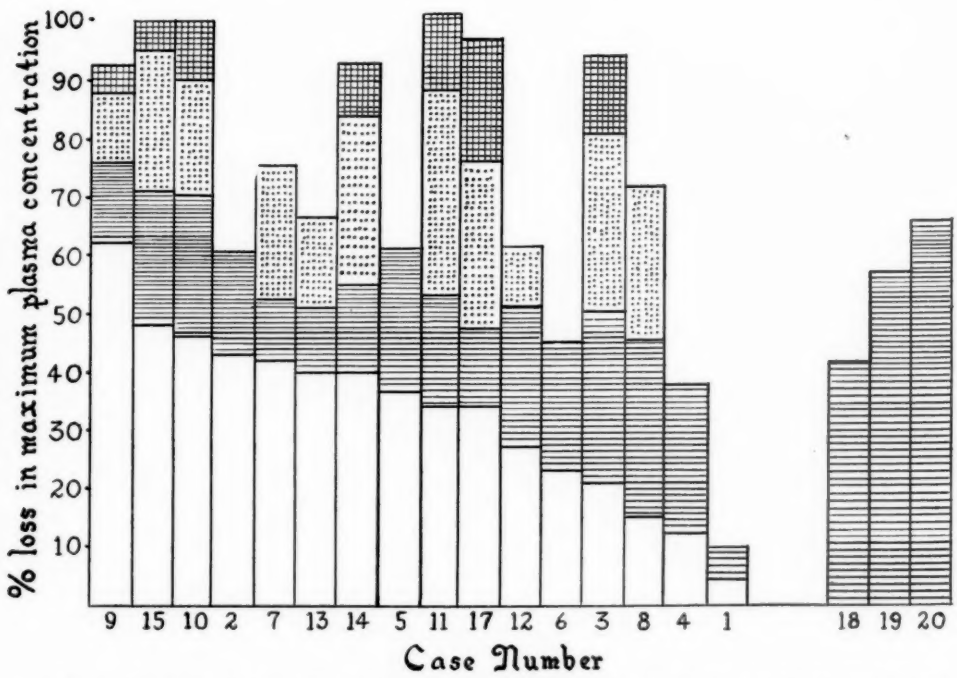

Fig. 3.—Showing the per cent loss in maximum plasma concentration at six, eight, twelve, and twenty-four hours in nineteen patients given a single oral dose of 1.0 Gm. of quinidine sulfate.

Blank, per cent loss at six hours; horizontal, per cent loss at eight hours; stippled, per cent loss at twelve hours; crosshatch, per cent loss at twenty-four hours.

fast before and after the dose; those on whom data are given in Fig. 2 ate the usual hospital diet. In both groups there was a considerable variation in the maximum levels attained, in the times of maximum concentration, and in the rates of fall. Maximum concentration was reached between two and four hours in 84 per cent of the cases studied. (Hiatt,[5] also using the Brodie colorimetric method, found the maximum concentration was reached from three to four hours after the oral administration of the drug.) No regular correlation between body weight and the maximum plasma concentration was observed. As for the marked

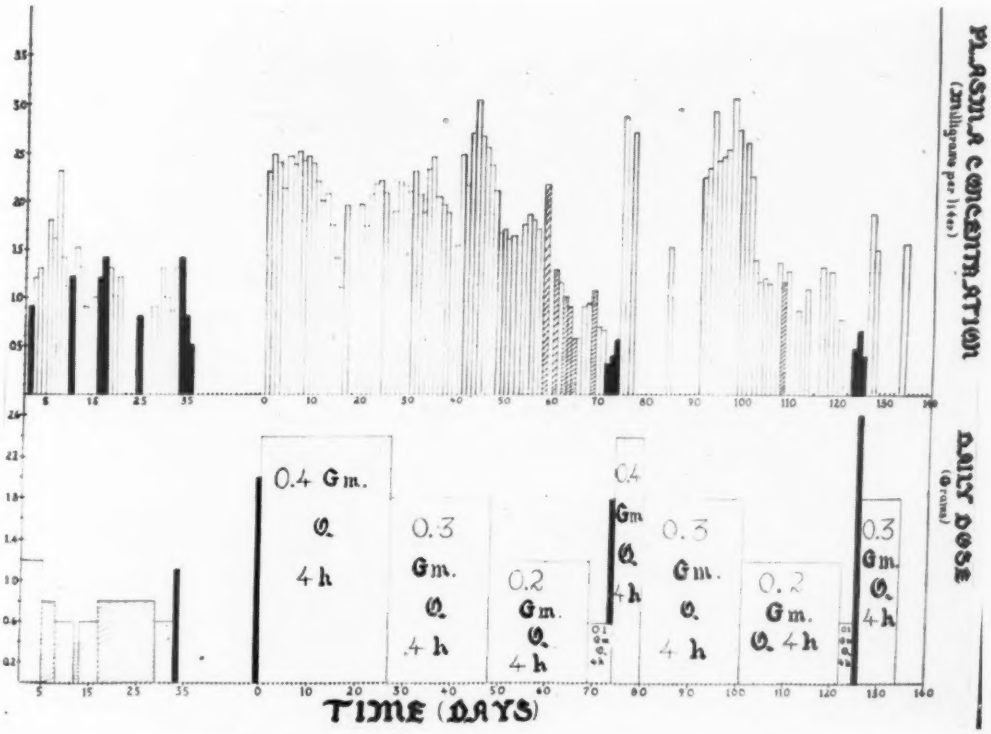

Fig. 4.—A 56-year-old white man, showing the relationship between dosage of quinidine sulfate, quinidine plasma concentrations, and the occurrence of nodal extrasystoles and paroxysmal nodal tachycardia. The diagonally lined blocks in the area of plasma concentration represent the occurrence of extrasystoles, while the solid blocks indicate the occurrence of paroxysmal nodal tachycardia. In the area of daily dose, the solid blocks represent single large doses of quinidine sulfate given to raise the plasma concentration rapidly.

Blank, dose every four hours; diagonal lines, dose every six hours; stippled, dose every eight hours; horizontal lines, dose every twelve hours.

variation in rates of fall (Fig. 3), by six hours the majority of levels had fallen between 20 and 40 per cent, with extremes from as low as 4 per cent up to as high as 62 per cent. By eight hours the fall was between 40 and 60 per cent, with extremes from 9 per cent to 75 per cent. Of the eleven patients whose levels were taken at twelve hours, all had fallen 60 per cent or more. At twenty-four hours, seven of these patients had levels which showed a fall of over 90 per cent in each. There was no apparent correlation between maximum plasma concentration and the rate of fall. Complete data for all patients is given in Table I.

2. *The Therapeutic Range of Plasma Concentration in Two Patients With Paroxysmal Nodal Tachycardia.*—Two patients with paroxysmal nodal tachycardia were studied to determine the correlation, if any, between the attack-rate frequency and various plasma quinidine concentrations. Both patients had

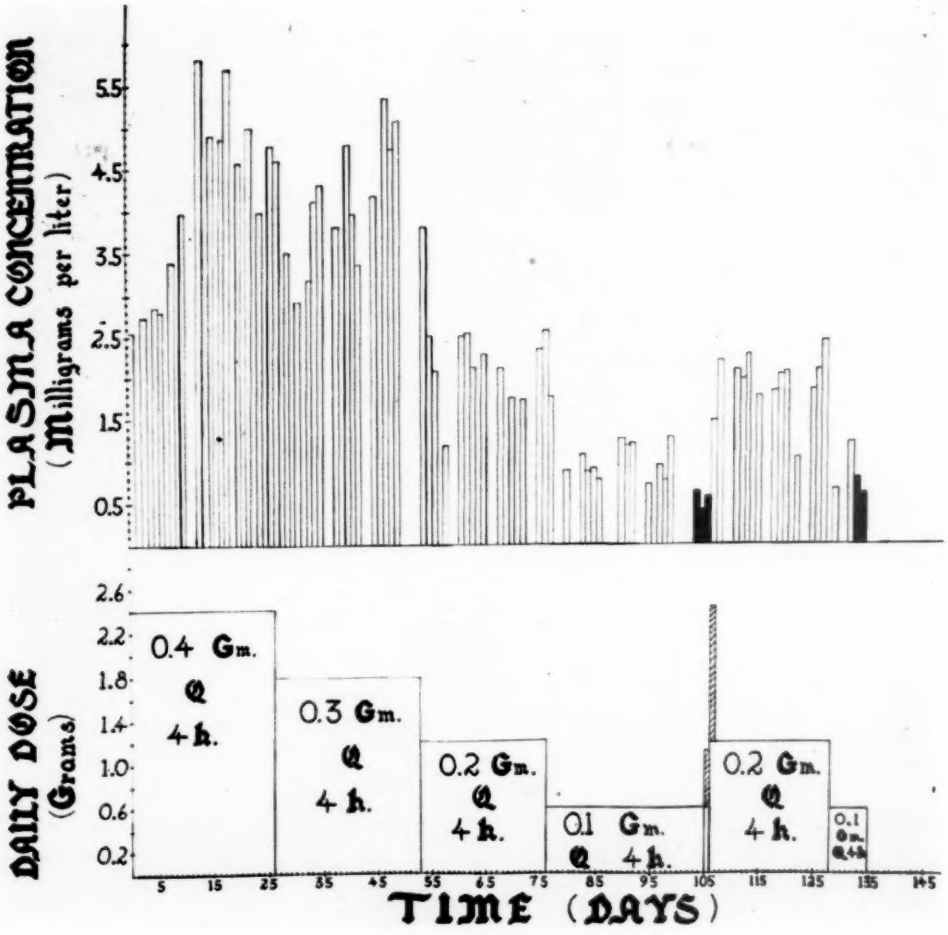

Fig. 5.—A 41-year-old white woman, showing relationship between daily dose of quinidine sulphate, plasma quinidine concentration, and the occurrence of paroxysmal nodal tachycardia. The solid blocks indicate these attacks. The diagonally lined blocks represent single large doses of quinidine sulfate given to raise the blood level rapidly.

been followed for some time before the present study was begun. One of these, G. B.,* was a man 56 years of age who had had documented paroxysmal nodal tachycardia for twelve years, with almost constant attacks for the previous three years whenever he was ambulatory. During the year preceding this study he had been unable to work. Tachycardia was even so frequent and marked that he was obliged to stop several times during his daily shave to sit down and rest. There was no evidence of organic heart disease. The other

*Plasma concentrations during the preliminary studies on this patient were determined by the fluorimetric method described by Brodie.[4]

patient, S. F., a woman 41 years years of age, had had attacks at least once every three weeks, and frequently they had come as often as several times a day over as long a period as a week or ten days. She also had no evidence of organic heart disease.

After a suitable control period was established, during which time the frequency of attacks was documented, quinidine sulfate was started and given to the patients every four hours at a set dosage so that a uniform daily total intake of the drug could be maintained for varying periods* (Figs. 4 and 5). Plasma quindine concentrations above 1.0 mg. per liter were coincident with absence of attacks. Dosages which produced plasmale vels below 1.0 mg. per liter resulted in a recurrence of frequent attacks. Correlation of attack onset and plasma level was easily reproducible in these patients. (As shown by Figs. 4 and 5, in the male subject the arrhythmia appeared when the plasma levels ranged between 0.32 and 0.76 mg. per liter, while attacks were present with plasma concentrations of between 0.28 and 0.84 mg. per liter in the female patient.) Although this data does not establish an absolute critical level for all such patients, it suggests that such a level exists. Determination of critical plasma quinidine levels by means of the methods outlined in this paper is suggested as a basis for rational approach to the control of paroxysmal tachycardia.

SUMMARY AND CONCLUSIONS

1. By the use of Brodie's colorimetric method for plasma quinidine concentration determinations, levels were run on a series of patients who had taken a single large oral dose of quinidine sulfate.

2. There is a marked individual variation in maximum plasma quinidine concentration following a large single oral dose.

3. The time of maximum plasma concentration varies widely in different patients, from forty-five minutes to four hours after administration.

4. The rate of fall of plasma quinidine concentration varies markedly from patient to patient and apparently bears no relationship to the initial maximum level.

5. The correlation between plasma quindine concentration and therapeutic effectiveness in two patients with paroxysmal nodal tachycardia is presented.

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*The occurrence of attacks in G. B. when both daily dose and the interval between successive doses was frequently varied is indicated in the first portion of Fig. 4. All the plasma levels were taken from three to four hours after the preceding dose and probably represented the peak concentrations attained on these schedules. Since there were undoubtedly much lower concentrations at six, eight, and twelve hours, the attacks may have resulted from these lower levels. Therefore, a four-hour schedule was initiated to prevent such wide fluctuations in plasma concentrations.

THE EFFECTS OF THE INGESTION OF LARGE AMOUNTS OF SODIUM CHLORIDE ON THE ARTERIAL AND VENOUS PRESSURES OF NORMAL SUBJECTS

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UNTIL recently the most widely accepted explanation of the pathogenesis of edema in acute glomerulonephritis was that, due to an increase in the capillary permeability throughout the body, there was an increased amount of transudation of fluid into the extracellular space. The evidence to substantiate this view was contained in the work of Beckmann,[1] who showed that the edema fluid in four patients with acute glomerulonephritis contained an increased amount of protein. These protein determinations were done by means of a refractometer. Recently, Warren and Stead,[12] using a much more accurate method, found no increase in the protein content of the edema fluid in ten patients with acute glomerulonephsitis. Thus, increased capillary permeability could not have been a factor in the production of edema in these patients and another explanation will have to be given.

In 1944 LaDue[9] made several very interesting observations in twelve patients with acute glomerulonephritis. He found edema, increased venous pressure, and cardiac dilatation in all of the twelve and interpreted these changes as being due to congestive heart failure most likely caused by the arterial hypertension. The question has arisen whether the picture presented by these patients is due to cardiac failure or is due to the abnormal retention of salt and water by the damaged kidneys. The question of the relationship of the salt intake to the level of arterial blood pressure will also be considered.

Grollman and co-workers[6] have shown that in certain cases of hypertension very rigid restriction of the sodium intake will cause a fall in blood pressure. However, Grollman, Harrison and Williams[7] demonstrated that an increase in the intake of sodium by hypertensive rats did not cause any further rise in arterial pressure.

In this study the effects of the ingestion of an excess amount of sodium chloride in normal adults was observed.

The subjects used were eight healthy medical students and physicians ranging in age from 18 to 31 years. They were permitted to continue their normal activities throughout the course of the experiment. After a control period of two to four days, the administration of 20 to 30 Gm. of sodium chloride per day, taken in the form of 1.0 Gm. enteric-coated tablets divided into four or five approximately equal doses, was started. No attempt was made to regulate the salt intake in the diet and fluids were allowed ad libitum.

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Aided by a grant from the Dazian Foundation and the John and Mary R. Markle Foundation.
Received for publication April 27, 1946.

TABLE I. CHANGES THAT FOLLOWED THE INGESTION OF LARGE AMOUNTS OF SODIUM CHLORIDE (FIRST THREE SUBJECTS)

DATE	WEIGHT (KG.)	VENOUS PRESSURE (MM. H_2O)	FLUID		URINARY CHLORIDES (24 HR.)	SERUM CHLORIDES (MEQ. L.)	BLOOD PRESSURE	REMARKS
			INTAKE (C.C.)	OUTPUT (C.C.)				
H. G.								
2/27	58.25	60					107/70	
2/28	58.50	75					104/62	
3/1	58.75	79					107/67	
3/2	58.75	—					106/66	20 Gm. NaCl q. d.
3/3	58.75	125					110/68	
F. R.								
2/27	68.25	88					110/64	
2/28	68.50	86					106/68	
3/1	68.50	88					120/77	
3/2	68.75	—					106/66	
3/3	69.25	123					117/74	20 Gm. NaCl q. d.
3/4	68.85	130					106/66	
3/5	69.50	150					110/64	
D. B.								
6/25	70.75	146	4,000	1,190	6.610			
6/26	71.00	170	4,620	1,465	7.250	106.2	116/72	
6/27	70.50	138	4,500	1,355	3.150		110/70	
6/28	71.00	164	3,550	2,310	5.280		108/72	
6/29	72.25	—	4,450	2,660	21.920		———	30 Gm. NaCl
6/30	71.50	175	4,310	2,930	33.480		115/70	30 Gm. NaCl
7/1	71.75	290	3,450	2,530	20.920	112.5		30 Gm. NaCl
7/2	71.25	—	2,480	1,870	17.350			
7/3	71.50	—	3,300	2,330	17.720			

TABLE II. CHANGES THAT FOLLOWED THE INGESTION OF LARGE AMOUNTS OF SODIUM CHLORIDE (LAST FIVE SUBJECTS)

DATE	WEIGHT (KG.)	VENOUS PRESSURE (MM. H_2O)	BLOOD VOLUME (C.C.)	PLASMA VOLUME (C.C.)	THIOCYANATE SPACE (C.C.)	HEMATOCRITE	PLASMA PROTEIN	PLASMA CHLORIDES (MEQ./L.)	24-HR. URINARY CHLORIDE —GM. (AS NaCl)	FLUID		BLOOD PRESSURE	REMARKS
										INTAKE (C.C.)	OUTPUT (C.C.)		
J. G.													
6/27	68.50	——							4,710	2,710	685	——	Control period
6/28	68.00	102							4.780	1,760	555	128/76	
6/29	67.50	——							4.350	2,690	520	——	
6/30	67.75	96	4,750	2,580	12,320	43.5	7.4	107.7	2,520	2,780	305	126/68	
7/1	——	——							——	3,440	1,305	——	30 Gm. NaCl
7/2	69.80	162							16.400	2,860	1,370	128/76	30 Gm. NaCl
7/3	68.90	154	5,470	3,280	13,900	40.0	7.4	111.0	20.010	2,140	1,030	122/75	15 Gm. NaCl
7/4	——	——							10.250	1,120	1,175		
7/5	68.10	104							8.560	2,310	670		
W. H.													
6/28	62.50	——								2,915	1,050	——	
6/29	62.50	98								——	——	110/74	
6/30	62.50	113	4,630	2,730	12,790	41.0	7.8	110.4		2,140	730	110/70	
7/1	63.40	——								3,360	1,020	——	30 Gm. NaCl
7/2	63.40	158								——	——	112/70	30 Gm. NaCl
7/3	——	134	5,460	3,380	15,280	38.0	7.6	111.9		——	——	120/70	15 Gm. NaCl
N. K.													
7/11	70.10	108	4,270	2,520	14,270	41.0	7.8	106.8	12.370	2,185	1,190	110/70	
7/12	68.90	——							11.550	2,210	1,820	114/70	
7/13	70.00	108							13.830	2,635	1,785	——	
7/14	70.30	126							21.690	3,540	1,765	110/66	25 Gm. NaCl
7/15	70.90	132							24.230	4,160	1,260	110/70	30 Gm. NaCl
7/16	71.30	138							24.580	3,110	1,580	112/70	30 Gm. NaCl
7/17	72.30	170	4,920	3,150	15.340	36.0	7.4	126.9	24.300	3,360	1,585	118/80	15 Gm. NaCl

7/18	71.40	—							10.640	2,185	2,035		
7/19	71.30	—							3.430	2,760	830		
7/20	70.90	—							10.860	2,190	1,250		
J. H.													
7/13	69.25	125	5,190	2,850	14,300	45.0	7.5		7.73	2,690	1,050	128/76	
7/14	70.40	—							7.46	3,040	1,150	116/72	
7/15	70.00	105							8.58	2,230	900	—	
7/16	70.25	133							13.14	3,040	1,250	114/70	20 Gm. NaCl
7/17	69.80	149							25.27	2,245	1,350	116/70	25 Gm. NaCl
7/18	69.80	150	4,870	2,920	17,560	40.0	7.0	100.8	17.74	2,490	950	130/74	12 Gm. NaCl
7/19	69.40	—							16.79	2,600	1,025		
7/20	69.00	—							10.99	3,380	900		
7/21	68.30	—							7.30	3,670	825		
7/22	—	—							8.18	2,070	730		
B. L.													
7/23	80.3	132								4,150	700	112/78	
7/24	80.5	—	4,980	2,690	14,600	46.0	8.1	108.0		4,930	895	122/82	
7/25	80.4	132								4,060	675	—	
7/26	80.5									7,070	905	—	25 Gm. NaCl
7/27	81.6	195								5,350	1,746	118/82	25 Gm. NaCl
7/28	82.0	193	5,390	3,120	16,150	42.0	7.8	110.7		3,140	1,805	118/90	12 Gm. NaCl
7/29	81.1									2,210	875	—	
7/30	78.8									4,420	875	112/78	
7/31	80.5									4,850	840		

All subjects were weighed every day at the same time in the postadsorptive state. Venous pressure was determined by the direct method after a rest period of approximately thirty minutes. At the same time, pulse rate and arterial blood pressure were recorded. In five of the subjects additional studies of the changes in body fluids were made. The daily fluid intake and urine output were measured. Blood volume determinations were carried out by the dye method, using T-1824.[3-5] The ampoules containing an accurately measured amount of dye, as devised by Gregersen,[4] were used. A period of ten minutes was allowed for mixing, and five samples were taken at ten-minute intervals in heparin-wet syringes. Simultaneously, changes in the volume of extracellular fluid were estimated by measuring the "thiocyanate space" according to the method of Crandall and Anderson,[2] employing the following formula[5]:

$$\text{"Available fluid"} = \frac{\text{CNS injected (mg.)} \times 100}{\text{CNS in blood (mg. \%)}}$$

Fifty minutes were allowed for mixing and all measurements were done in duplicate. The plasma chlorides were calculated by the titration method. Determinations of the hematocrit and of the total serum proteins were made. In three of these subjects, the twenty-four hour urinary chloride output was measured.

The data obtained are presented in Tables I and II. The first two subjects in Table I (H. G. and F. R.) took sodium chloride for a period of two weeks, but since no essential change in the weight nor venous pressure was noted after the fourth day, the subsequent subjects were given salt for three or four days only.

TABLE III. CHANGES OBSERVED DURING THE PERIOD OF HIGH SODIUM INTAKE

SUBJECT	WEIGHT (KG.)	VENOUS PRESSURE (MM. H_2O)	PLASMA VOLUME (C.C.)	R. B. C. VOLUME (C.C.)	BLOOD VOLUME (C.C.)	THIOCYANATE SPACE (C.C.)	PLASMA CHLORIDE (MG.)
H. G.	+0.25	+50					
F. R.	+1.00	+64					
D. B.	+0.75	+126					
J. G.	+1.15	+58	+700	+200	+900	+1580	+3.3
W. H.	+0.90	+21	+650	+180	+830	+2490	+1.5
N. K.	+2.20	+62	+630	+20	+650	+1070	+20.1
J. H.	+0.55	+25	+70	−390	−320	+3260	——
B. L.	+1.50	+61	+430	−20	+410	+1550	+2.7

In Table III are listed the changes which took place during the high sodium chloride intake. In the five subjects on whom more complete circulatory measurements were made, changes were calculated from the data on those days on which the blood volumes were determined. In the remaining three subjects, the last day of the control period and the day of the maximal change in venous pressure were taken for comparison.

All of the subjects showed a gain in weight which varied from 0.25 to 2.20 kilograms. Changes in the venous pressure from +21 to +126 mm. of water

were observed.* Changes in the plasma volume were from + 70 to + 700 c.c.; in the blood volume from −320 to +900 c.c.; and in the "thiocyanate space," from +1,070 to +3,260 cubic centimeters. There were no significant alterations in the arterial blood pressure. The changes observed are presented in graphic form in Fig. 1.

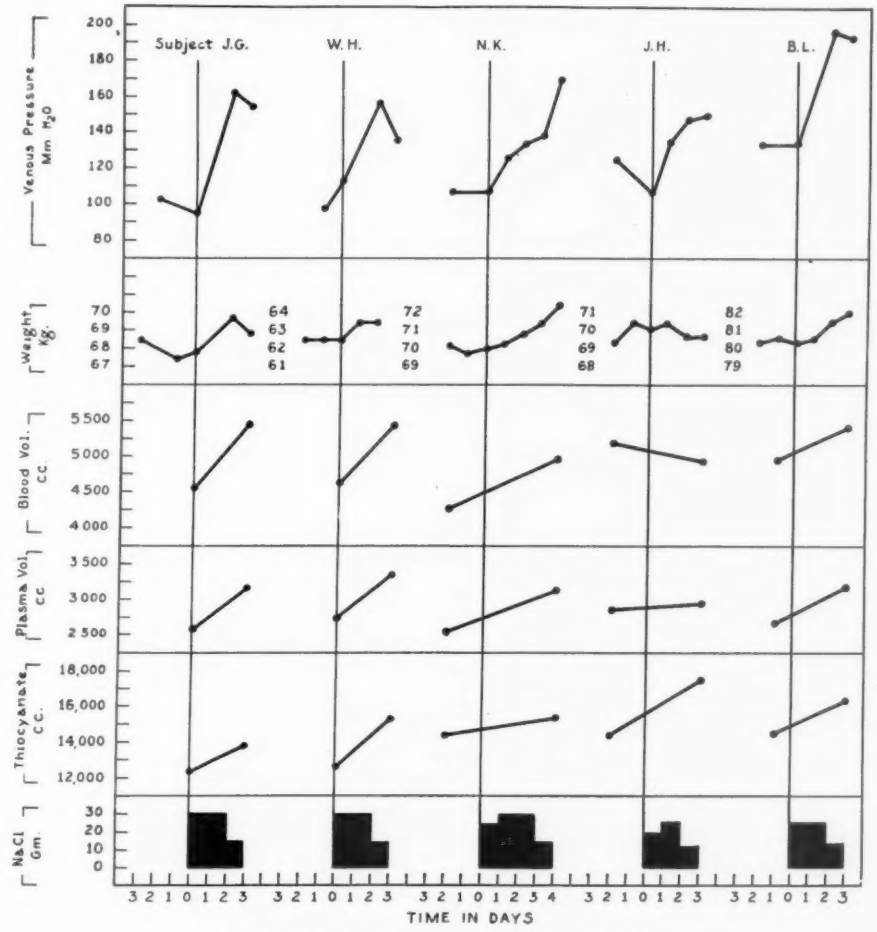

Fig. 1.—Effects of ingestion of sodium chloride.

The variation in venous pressure during the period between two doses of salt was studied. In the first experiment venous pressure curves were done with the subjects (F. R. and H. G.) in a recumbent position. After the administration of salt for several days, each subject took 6 Gm. of sodium chloride and 660 c.c.

*The rise of 126 mm. was observed in subject D. B., an apparently healthy medical student. The control readings ranged from 138 to 170 mm. of water. His past history was negative with regard to cardiovascular and renal disease; findings on physical examination were normal, and teleroentgenography and fluoroscopy of the heart and great vessels revealed no abnormal findings. Urine analysis and Fishberg concentration test were normal.

of water by mouth, and venous pressure readings were taken at frequent intervals through a needle which was left in place and kept patent by a 5 per cent glucose drip at the rate of 15 drops a minute. The same experiment was later repeated but with the subjects ambulatory between venous pressure readings done by multiple venepunctures. The results are presented in Fig. 2. There was a striking difference in the behavior of the venous pressure in the two experiments.

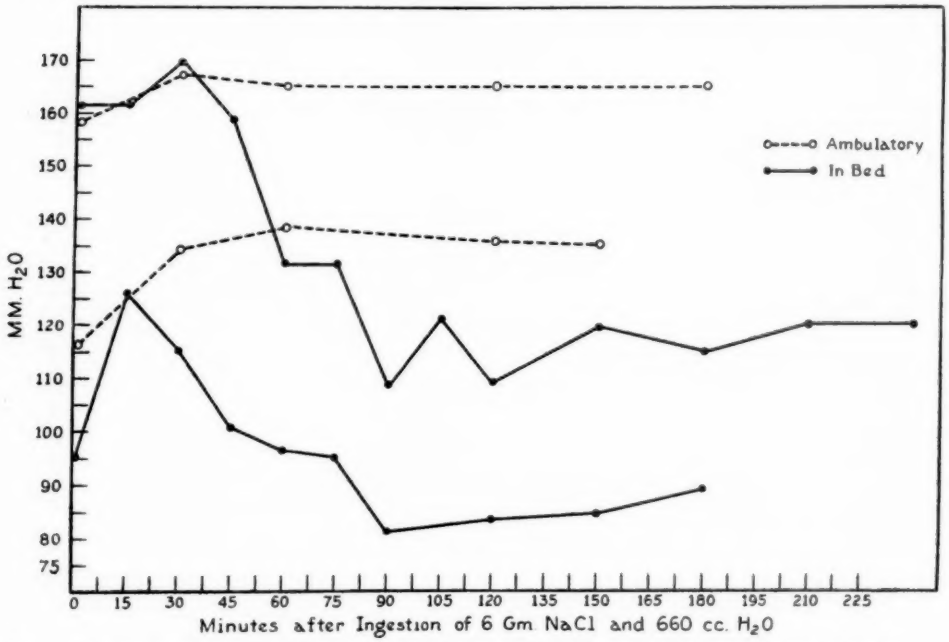

Fig. 2.—Venous pressure curves after single oral dose of sodium chloride during high salt intake.

With the subjects recumbent there was a short initial rise followed by a sustained drop to a level below the initial reading, and both subjects had a diuresis throughout the experiment of approximately 1,200 c.c. each. If the subject remained ambulatory between venepunctures, the initial rise in venous pressure was well sustained and diuresis did not occur.

None of the eight subjects showed a significant change in arterial blood pressure as a result of the increased intake of sodium chloride.

DISCUSSION

A very similar experiment to that reported here was carried out by Lyons, Jacobson, and Avery.[11] In seven subjects, after taking 40 Gm. of sodium chloride in forty-eight hours, the average weight gain was 1.9 kg. and the average rise in venous pressure, 31 millimeters. These results are quite similar to those observed in this experiment where the average weight gain was 1.04 kg. and the average rise in venous pressure, 59 millimeters. The amount of salt was greater and the duration of observation longer in this present study.

It is evident that when a normal person ingests an excess of sodium chloride and remains ambulatory, the kidneys do not excrete it all, and the isotonicity

of the body fluids is maintained by a retention of water and a subsequent increase in the blood volume and volume of extracellular fluid. The change in plasma protein is much less than the expected fall due to the increase in plasma volume, as noted also by Lyons, Jacobson and Avery.[11] This is evidently due to quick mobilization of plasma proteins from storage depots, so that there is actually an increase in the total circulating protein. This rise helps maintain an increased blood volume and the higher venous pressure observed.

In patients with acute glomerulonephritis, during the development of edema there is oliguria and, perhaps, anuria. The question as to which is primary, the edema or the oliguria, remains to be answered. In the twelve patients reported on by LaDue,[9] all had edema, increased venous pressure, and cardiac dilatation. He interpreted these changes as being due to congestive heart failure brought on by the acute hypertension. However, all of his patients had normal or fast arm-to-tongue circulation times, and the dyspnea and orthopnea were not as prominent symptoms as would be expected if the heart failure were caused by hypertension. It is quite possible that the changes observed in some patients with acute glomerulonephritis are related to the changes seen in normal subjects who are fed an excess of sodium. The latter group showed an increased blood volume, increased extracellular fluid, and a rise in venous pressure.

There have been very few observations on the blood volume in acute glomerulonephritis. The most extensive series was reported by Litzner,[10] who measured the blood volume by use of a dye method in six patients with acute glomerulonephritis while edema was present and again after diuresis. All of these patients showed an increased blood volume which then fell to normal levels when they became free of edema. Calculations of the heart volume were made in five of these patients and all had cardiac dilatation which disappeared when the blood volume became normal. Harris and Gibson[8] reported the blood volume of four patients with acute glomerulonephritis but did not mention the presence or absence of edema. Only one determination was done and the result compared with expected blood volume as calculated from the patient's height. Two of their patients were found to have normal blood volumes. The other two showed blood volumes which were low, but both of these patients had plasma albumin levels which were very low.

We have recently observed two cases of acute glomerulonephritis. Both of these patients had high venous pressures while edema was present; after diuresis the venous pressure returned to normal levels. However, the fall in blood volume in both of these patients after the edema had disappeared was rather small: 100 c.c. in one instance and 200 c.c. in the other. Neither patient complained of dyspnea nor orthopnea.

In acute glomerulonephritis there is an oliguria which at least in some patients may be due to the pathologic changes in the kidneys. Water and salt are retained, with a subsequent rise in blood volume, venous pressure, and volume of extracellular fluid. The increase in heart size in these patients may be due to the increase in blood volume and venous pressure and greater diastolic filling. That true congestive failure with pulmonary congestion, gallop rhythm, and pro-

longed circulation time occurs in some cases of acute glomerulonephritis is not denied. However, in those patients who do not show pulmonary congestion, gallop rhythm, nor prolonged circulation time, it seems not unlikely that the abnormal degree of hydration observed in acute glomerulonephritis is, for the most part, caused by the retention of salt and water by the diseased kidneys rather than by cardiac decompensation. Up to the present time, blood volume studies have not given convincing evidence for this hypothesis.

As has already been observed in rats,[7] an increase in the intake of sodium, at least in the doses indicated, does not cause any significant change in the arterial blood pressure.

CONCLUSIONS

1. Normal adults show an abnormal state of hydration when fed an excess of sodium chloride. This state is characterized by an increase in blood volume, venous pressure, and volume of extracellular fluid and may closely simulate the phenomena observed in congestive heart failure.

2. It is suggested that the edema in those patients with acute glomerulonephritis who do not exhibit pulmonary congestion, gallop rhythm, nor prolong circulation time is caused by the retention of salt and water by the diseased kidneys. This also leads to an abnormally high degree of hydration in which there is increased blood volume, venous pressure, and volume of extracellular fluid.

3. The addition of 20 to 30 Gm. of sodium chloride daily to the diet of normal adults does not cause any significant change in the arterial blood pressure.

The authors wish to express their appreciation to Dr. Tinsley R. Harrison for his help and guidance in this study.

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ELECTROCARDIOGRAPHIC PATTERNS IN PENETRATING WOUNDS OF THE HEART

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INTRODUCTION

INTERPRETATION of the electrocardiographic patterns following penetrating wounds of the heart is both interesting and difficult because of the several factors which may influence the electrocardiogram. The first of these is the localized myocardial lesion produced by the wound itself. Its electrocardiographic effects might be expected to be unique since there is no exactly comparable lesion in the various diseases of the heart. Pathologically it resembles myocardial infarction more than anything else but may be much smaller, usually occurs in an otherwise normal heart, and often involves the right ventricle which is rarely affected in myocardial infarction. A second factor which is practically always present is pericarditis. The mere opening of the pericardium at operation or the presence of blood or of infection in the pericardial sac may cause pericarditis. In contrast to the unpredictable effects of the wound, the patterns produced by pericarditis are quite characteristic, particularly in the acute stage. However, even recently these effects have been attributed mistakenly to the wound itself, and the role of pericarditis has not been recognized. A third factor which is present in some cases is an area of myocardial infarction due to laceration or ligation of a sizeable coronary artery, nearly always the descending branch of the left coronary artery. The combined electrocardiographic effects of the second and third factors are paralleled in previously reported instances of clinical myocardial infarction complicated by pericarditis[1] and experimental myocardial infarction.[2]

In addition, several other attendant conditions may influence the electrocardiogram. These are shock, anemia, changes in the position of the heart due to air or fluid in the pleural spaces, and, rarely, the coincidental presence of chronic cardiac disease. With the exception of the last condition, these effects are nearly always transient and of insufficient extent to cause confusion in the interpretation of serial tracings.

The possibility of recognizing the changes due to individual factors in these combined patterns has an important bearing upon certain questions about which there has been a diversity of opinion. The fundamental and most difficult of these is whether the wound produces characteristic changes and so may be recognized and located from the electrocardiogram. The question of whether injury

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Received for publication May 13, 1946.

to major branches of the coronary arteries with resultant myocardial infarction becomes apparent in the electrocardiogram is a part of the consideration of localizing findings in such cases. The second question is how often and at what stages the effects of pericarditis appear. Upon the answers to these questions depend certain practical decisions such as the diagnostic value of the electrocardiogram during the preoperative or early period and its subsequent usefulness as a guide to therapy and prognosis. Furthermore, these electrocardiographic effects are of considerable theoretic interest, particularly those following wounds of the right ventricle.

The purpose of this report is to offer a brief analytic review of the literature, some of which is not generally available, to present the electrocardiographic findings in a group of twenty-three patients, and to correlate these with the results of clinical observations in eight patients re-examined after an average period of nineteen months following the cardiac wound.

REVIEW AND ANALYSIS OF THE LITERATURE

GENERAL SCOPE AND CONTENT.—The electrocardiographic changes following wounds of the heart are described in slightly over one hundred cases in the literature available to me. Fifty articles contain reports of single cases.[3-52] Thirty cases are included in the article by Herve and Forero Sarabia.[53] McGuire and McGrath[54] describe the findings in eleven cases, in one of which the electrocardiograms are published. The remaining cases appear in groups of from two to four.[55-64] There are five articles[19,31,48,58,65] containing reviews of cases, of which that of Solovay and co-workers,[31] listing the electrocardiographic findings in seventeen cases, is the most extensive.

From the standpoint of analysis of the findings, the seventy cases[3-35,53,58] in which the electrocardiograms are satisfactorily reproduced are the most valuable ones. However, the studies in many of these cases are incomplete in one or more respects. In twenty-two only one electrocardiogram is recorded. In thirteen the early changes do not appear since the first electrocardiogram was not taken until after the first week. Precordial leads were taken in only twenty-two, and in all of these only a single precordial lead was employed. The most outstanding lack is the paucity of long-term studies. Whereas thirty-one cases were followed for three months or longer, only thirteen were followed for more than six months.

THE ROLE OF PERICARDITIS.—The first definitive studies of the electrocardiographic changes in pericarditis of various etiologic types appeared in 1929.[66] In 1934 the pathogenesis and evolution of the complete series of changes during both acute and subacute stages were greatly amplified.[67] It is now well known that pericarditis in both the acute and subacute stages produces electrocardiographic changes which may closely resemble those of myocardial infarction. The first report in the English literature of electrocardiograms following wounds of the heart appeared in 1924,[8] before the studies just mentioned and during a period of intense interest in the patterns following myocardial infarction. It is apparent, therefore, why these tracings following cardiac wounds were thought to be reflections of the myocardial lesion and why the role of pericarditis was not

appreciated. However, a definite lag is indicated by the fact that since 1930 at least fifteen reports[6,13,19,21,23,25,28,33,34,40,41,43,51,63,64] have appeared in which interpretations of the electrocardiographic findings were made, but in which the effects of pericarditis are not mentioned. Eight of these have been published since 1938. This oversight has caused a great deal of confusion.

The first mention of pericarditis as a factor in the electrocardiogram following cardiac wounds occurred in the report by Elkin and Phillips[55] in 1931. The following year Porter and Bigger[57] felt that they had excluded pericarditis as a factor in their two patients because a pericardial effusion was absent in one and did not parallel the electrocardiographic changes in the other. They based this opinion on the then-prevailing concept that pericarditis produced its electrocardiographic effects only because of generalized myocardial ischemia created by the pressure of the effusion on the heart and coronary vessels. In 1933 Eakin[11] and in 1934 Davenport and Markle[10] reported cases in which the tracings were explained in this manner. Schwab and Herrmann[30] included a case of a bullet wound of the left ventricle in their studies on the electrocardiogram in pericarditis and first pointed out that the inversion of "coronary" contour of the T waves during the subacute phase of pericarditis was related to the inflammatory process in the subepicardial myocardium. In 1937 Vanderveer and Norris[32] stated, "The progressive changes in many cases of stab wounds of the ventricle suggest pericarditis rather than a single anterior lesion of the myocardium." The main thesis in this general article on pericarditis was that their pathologic studies showed that RS-T segment elevations as well as T-wave changes depended upon subepicardial myocarditis and that intrapericardial fluid caused inconstant electrocardiographic changes. Wood[65] expressed the tentative idea that pericarditis or right ventricular injury accounted for the changes following wounds of the right ventricle, while those following left ventricular wounds were due to the localized myocardial damage. In 1938 the present author[68] (and later with Barnes[69]), from a review of the published electrocardiograms in cardiac wounds, pointed out the superimposition of changes due to pericarditis upon those due to the wound and, in some cases, also upon the patterns of myocardial infarction from injury of a coronary artery. Winternitz and Langendorf[58] stated that the electrocardiographic changes following cardiac wounds were most often and most noticeably due to the pericardial reaction and that the direct cardiac injury seldom influenced the electrocardiogram. In 1940 Forero Sarabia[70] and Parade and Rating[56] emphasized the prominent part payed by pericarditis and its effect in obscuring the changes due to the wound. Solovay and co-workers[31] in 1941 recognized the preponderant influence of pericarditis during the first two weeks, but after this period ascribed the inversions of the T waves to the myocardial injury.

In 1943 Herve and Forero Sarabia[53] drew practically the same conclusions. Their description of the incidence and the types of early changes due to pericarditis agrees so well with other cases in the literature that it serves adequately as a summary of these effects of pericarditis. They found that electrocardiographic evidences of pericarditis were present in twenty-seven of their thirty

patients. The elevated, concave RS-T segments occurred at variable periods. They were present during the first six hours postoperatively in four of nine patients. During the six- to twenty-four hour period they were found in nine of ten patients. After the eighth day the frequency of elevation of the RS-T segments lessened progressively, and they became isoelectric and convex in contour. The T waves, previously upright and often exaggerated in the leads in which elevation of the RS-T segments had occurred, became flattened and then inverted, beginning at the end of the first week and continuing during the second week. At the end of this period 85 per cent of their records showed negative T waves in some or in all of the leads in which they were previously positive. The inversion of the T waves occasionally appeared first in the precordial lead but usually occurred more or less simultaneously in all leads.

Other authors also,[4,10,12,15,24,35,38,52,54] especially in recent years, have mentioned the role of pericarditis.

LOCALIZING FINDINGS.—

General Review of the Literature.—In 1935 Koucky and Milles[19] stated: "From the standpoint of the electrocardiographic changes resulting from wounds on the anterior surface of the heart, the picture varies but little from case to case, regardless of the presence or absence of involvement of the large coronary vessels or of the region of the anterior surface of the ventricle damaged." In 1937 Wood[65] asserted that if the wound was situated in the anterior part of the left ventricle toward the apex, or if the anterior descending branch of the left coronary artery had been ligated, the electrocardiogram usually showed the "classical T_1 pattern" and therefore was almost certainly directly due to the myocardial injury; if, however, it was situated in the anterior right ventricle, the electrocardiogram conformed to "the T_2 pattern," with early elevation of the RS-T segment, especially in Lead II, with later inversion of the T waves in all three leads. He tentatively explained these latter changes either on the basis of the hemopericardium or possibly as the direct effects of anterior right ventricular injuries.

In 1938 Winternitz and Langendorf[58] noted that the cardiac wound itself seldom influences the electrocardiogram, although changes due to myocardial infarction are apparent in some patients in whom the coronary arteries are involved. However, since in their opinion normal coronary arteries withstand ligation better than sclerotic ones, they felt that the electrocardiogram shows only whether or not a cardiac or pericardial lesion is present without indicating with certainty its site or whether or not a coronary vessel is involved. In the same year the present author[68] (and later with Barnes[69]) found that when the reported cases are divided into two groups, those patients with and those without injury to major coronary vessels, certain differences become apparent. Since these cases are included in the present analysis, this point will be amplified later.

In 1940 Forero Sarabia[70] declared that the electrocardiographic effects of pericarditis "make impossible or hamper a localizing electrocardiographic diagnosis . . . Such a diagnosis is possible only occasionally when the electrocardiogram has been obtained immediately after the surgical intervention or

long enough afterward so that the signs of pericarditis have disappeared." In 1941 several authors commented on the presence or absence of localizing findings. Bean[4] reported a case of a bullet wound of the heart with ligation of the anterior descending branch of the left coronary artery and recognized changes which he felt were due to the combined effects of pericarditis, operative trauma, and the bullet wound. Q-wave patterns suggesting damage to both anterior and posterior surfaces of the left ventricle were present. Solovay and co-workers,[31] from a review of the electrocardiograms in seventeen cases, including one case of their own, agreed with Wood's idea as to the existence of a "T_1 pattern" in left ventricular wounds and a "T_2 pattern" in right ventricular wounds. They felt that inversions of the T waves after two weeks were due to the myocardial injury and therefore could be used in its localization. McGuire and McGrath[54] stated in a brief report that in their eleven patients, "the electrocardiographic changes were similar whether the right or left ventricle was injured and had no localizing value . . . The electrocardiograms in two patients in whom the anterior coronary artery and vein were ligated were similar during the first week after operation to the records of the other patients." The electrocardiograms of only one patient in their series are published and the other tracings are not described in detail.

The impossibility of evaluating localizing changes when the pattern of pericarditis is not appreciated is illustrated by Caviness and Turner's[6] report in 1943 of a wound of the left auricle, in which they stated that "electrocardiographic changes incident to injury of the auricles are not essentially different from those caused by injury to other portions of the myocardium such as occur after coronary occlusion." Their series of electrocardiograms showed no changes in the P waves and no Q-wave patterns, whereas the T waves were inverted and "coronary" in contour in the three standard leads—a finding characteristic of pericarditis. Zerbini[35] reported on a patient with a right ventricular wound in whom the descending branches of the left coronary artery and vein were ligated about 4 cm. above the apex. He stated that the curves did not reflect myocardial infarction since there was no Q wave in the precordial lead. In the published precordial electrocardiograms the R and S waves are of equal amplitude, probably indicating that the electrode was placed over the anteroseptal portion of the left ventricle. This case is of interest since it may be comparable with instances of anterior myocardial infarction in which multiple precordial leads show Q waves in one or a few leads but not in others. Herve and Forero Sarabia[53] modified the previously quoted statement of the latter of these two authors by pointing out that the study of localizing patterns permits a general idea of common distinctive characters among different groups, left ventricular wounds generally causing alterations in T waves in Leads I and IV which are more marked and more persistent than the changes in the T waves in Leads II and III. In right ventricular wounds they sometimes found abnormalities of T_1 and T_4 but noted that these changes tended to regress during the second month, whereas the changes in T_2 and T_3 persisted for a longer time. Three of fourteen right ventricular wounds showed either complete or incomplete right bundle branch block. P-wave

changes of questionable extent occurred in two of the five auricular wounds. In all, eleven of twenty-seven patients presented signs definitely suggesting the location of the wound. In many of the remaining patients only one or a few electrocardiograms were taken. Among eleven patients there was frequently a discrepancy between the location described at operation and that found at autopsy. The most common error was to mistake right ventricular for left ventricular wounds. This observation is important because it may explain discrepancies in some cases between localizing electrocardiographic patterns and the supposed location of the wound.

Analysis of Localizing Findings in Electrocardiograms Depicted in the Literature.—There are several inherent difficulties in an analysis of localizing findings in electrocardiograms depicted in the literature. The first of these is that the true incidence of localizing patterns can be only roughly estimated because the electrocardiographic studies are often incomplete in one or more respects. The second is, as pointed out by Herve and Forero Sarabia,[53] that the surgeon's description of the location of the wound cannot be relied upon completely. The third is, during a considerable period of time, that the effects of pericarditis may obscure localizing findings. To avoid this last difficulty, it has been suggested that tracings taken either very early or considerably later when these effects have disappeared should be the most valuable. This suggestion has been adopted in the present analysis though with certain reservations which will be mentioned.

Cases With Early Electrocardiograms: Table I shows an interpretation of the findings in thirty-one cases depicted in the literature with tracings taken during the first twenty-four hours. The word localizing has been used thus far to indicate changes pointing to the particular part of the heart involved by the wound. In this sense there are only two patterns which have localizing value at this stage. The first of these is that of myocardial infarction. When this is present, it indicates that the wound is in one or the other ventricle but near enough to the coronary artery, nearly always the anterior descending branch of the left, so that this artery is involved in the wound or during its suture. Among the seven patients in the first group in Table I, this was proved to be present in six and considered very probable in the seventh. In three of these, a definite pattern of anterior infarction consisting of a reciprocal depression of the RS-T segment in Lead III, measuring 2 mm., is present. In three of the other four patients, similar though less deep reciprocal depressions occurred, but because of the fact that in a few instances acute pericarditis may show slight RS-T depressions in Lead III, these three cases are classified as suggestive rather than diagnostic of anterior infarction. One other case is classified as suggestive of infarction because of the presence of a Q wave in Lead I. In only one of these seven patients was a precordial lead obtained during the first twenty-four hours, and in this patient[4] the Wolferth lead showed a small Q wave which would be equivalent to a small R wave in the precordial leads now in use. The absence of the pattern of infarction in three preoperative tracings is due to the fact that this occurred as a result of ligation of a coronary artery during the operation.

TABLE I. INTERPRETATION OF ELECTROCARDIOGRAPHIC FINDINGS IN THIRTY-ONE CASES DEPICTED IN THE LITERATURE WITH TRACINGS OBTAINED DURING THE FIRST TWENTY-FOUR HOURS.

GROUP	NUMBER OF CASES	DEFINITE FINDINGS			SUGGESTIVE FINDINGS			NON-SPECIFIC MYO. DAM.	NORMAL
		INFARCT.	B.B.B.	PERICARD.	INFARCT.	B.B.B.	PERICARD.		
Ventricular wounds with known or probable involvement of the left coronary artery	7	3 (**12, 16,** 27)			4 (4, 9, 55 (Case 1) 57 (Case 1))		2 (**55 (Case 1) 27**)	1 (**9**)	
Right or left ventricular wounds without known involvement of a coronary artery	17		2 (**10,** 53 (Case 2))	9 (5, 19, 21, 53 (Cases 4, 8, 20, 22) 54 (Case 1) 57 (Case 2))		1 (53 (Case 3))	2 (53 (Cases 3, 21))	3 (53 (Cases 12, 21, 22))	3 (33, 53 (Cases 6, 9))
Wounds of both right and left ventricles	1		1 (17)						
Atrial wounds	4			2 (**11,** 53 (Case 26))			1 (15)	1 (32 (Case 5))	
Unknown location	2							1 (58 (Case 22))	1 (30 (Case 7))
Totals	31	3	3	11	4	1	5	6	4

Infarct., Infarction; B.B.B., bundle branch block; Pericard., pericarditis; Myo. Dam., myocardial damage.

Numbers within parentheses refer to the numerical order of the articles in the list of references. The reference numbers printed in heavy type indicate that the electrocardiographic finding described appeared in a preoperative tracing shown in the article. Dotted lines connect multiple tracings within first twenty-four hours. In three other cases two possible interpretations are listed for each. The total of interpretations thus exceeds the number of cases.

TABLE II. ELECTROCARDIOGRAPHIC FINDINGS AMONG THE TWENTY-THREE CASES WITHOUT LIGATION OF A CORONARY ARTERY FOLLOWED THREE MONTHS OR LONGER DEPICTED IN THE LITERATURE

REFERENCE	NUMBER OF LEADS	TYPE OF FINDING	TIME OF FOLLOW-UP (MONTHS)	NUMBER OF PATIENTS
		A. Left Ventricular Wounds (Seven Cases)		
3, 31, 55 (Case 2)	3, 3, 3	Normal electrocardiogram	4, 4, 6	3
53 (Case 17)	3	Inverted T_1 and T_2; Q_1	10	1
18	3	Inverted T_1; Q_1	10	1
3	3	Diphasic T_1	3	—
21	3	Low T_1; notched QRS	6½	1
53 (Case 22)	4	Low T_1; inverted T_4	3	1
		Rounded T_4; elevated S-T_4; small R_4; low voltage	7	
		B. Right Ventricular Wounds (Twelve Cases)		
14, 19, 20, 33	3, 3, 3	Normal electrocardiogram	3, 4, 4,	6
53 (Case 12), 54 (Case 1)	3, 4, 4		5, 5, 17	
8	3	Right bundle branch block	3	1
53 (Case 14)	4	Right bundle branch block; low T_1; inverted $T_{2, 3, 4}$; $R_4 > S_4$	4	1
28	3	Diphasic T_1; inverted T_2 and T_3	5½	1
54 (Case 1)	4	Inverted T_2 and T_3; $R_4 > S_4$	3	—
53 (Case 9)	3	Isoelectric T_2; inverted T_3	3	1
57 (Case 2)	3	Isoelectric T_1	4	1
34	4	Inverted T_4; ? T_2; inverted T_3; $S_4 > R_4$	5	1
		C. Auricular Wounds (Three Cases)		
6	4	Normal electrocardiogram	3	1
11	3	*Isoelectric $T_{1, 2, 3}$; low voltage	6	1
53 (Case 26)	4	Isoelectric $T_{1, 2, 3}$; T_4 low up	3	1
		D. Right and Left Ventricle (One Case)		
23	3	Normal electrocardiogram	6	1
		E. Total Cases (Twenty-Three)		
		Normal electrocardiogram	5.5 (Av.)	11
		Abnormal electrocardiogram	5.6 (Av.)	12

> Indicates that amplitude of the deflection preceding the sign exceeds that of the deflection following it. The brackets connect cases studied at more than one time after the three-month period.
*Probable chronic pericarditis.

The second localizing finding in these early tracings is that of bundle branch block. This was always a right bundle branch block and in all instances, except one in which wounds were present in both ventricles, the right ventricle was the site of the wound. Since, in several other patients reported on in the literature and in two patients in the present series, the right ventricle was always involved by the wound when this pattern was present, it is considered to be of localizing significance.

Other than these two types of localizing patterns, there are no findings at this time which indicate the part of the heart involved. The degree or location of elevations of the RS-T segments or abnormalities of the T waves are not distinctive of a particular location. It is apparent that since definite electrocardiographic evidences of pericarditis are present in eleven patients, pericarditis is capable of obscuring localizing patterns even at this early stage. However, if the word localizing is used in the broader sense of evidence of involvement of any part of the heart, then pericarditis may be considered as a localizing finding. Including it, there are only ten of the thirty-one patients in whom there is neither definite nor suggestive evidence of cardiac or pericardial involvement. Of these ten, six showed nonspecific changes which might be expected to result from shock or anemia, and in four the tracings were within normal limits.

Cases With Late Electrocardiograms: For reasons to be commented upon later it seems desirable to consider only those in which tracings were obtained three months or later following the wound. Table II shows the patterns observed in the twenty-three patients without known coronary involvement. There are five wounds of the left ventricle associated with electrocardiographic abnormalities

TABLE III. ELECTROCARDIOGRAPHIC FINDINGS AMONG THE EIGHT CASES WITH LIGATION OF THE LEFT CORONARY ARTERY OR ITS BRANCHES FOLLOWED THREE MONTHS OR LONGER AND DEPICTED IN THE LITERATURE

REFERENCE	NUMBER OF LEADS	TYPE OF FINDING	TIME OF FOLLOW-UP (MONTHS)	NUMBER OF PATIENTS
		A. Left Ventricular Wounds (Three Cases)		
57 (Case 1)	3	Normal electrocardiogram	3	1
12	4	Low T_1; diphasic T_4; small Q_1; $R_4 = S_4$	7	1
9	4	Low T_1; inverted T_4; Q_4; $S_4 > R_4$	6	1
		B. Right Ventricular Wounds (Five Cases)		
8, 55 (Case 1)	3	Normal electrocardiogram	3, 8	2
35	4	Inverted T_4 ($R_4 = S_4$)	8	1
4	4	Isoelectric T_2; inverted T_4; Q_4 RV x-systoles	13	1
22	3	Diphasic T_1; Q_1 and Q_2	48	1

x—systoles, extra or premature systoles.

persisting for three months or longer. In one of these the electrocardiogram became normal subsequently. All show involvement of the T wave in Lead I, and only one showed involvement of T_2. On the other hand, four of the five right ventricular wounds with persisting abnormalities other than right bundle Branch Block show altered T waves in Leads II and III, whereas only two show altered T waves in Lead I. The location of the single precordial electrodes in these patients is presumably at the cardiac apex or in the midclavicular line. As judged by the relative amplitudes of the R and S waves, the electrode was most frequently near a point over the interventricular septum where both right and left ventricular events might influence the direction of the T waves.

Table III shows the electrocardiographic findings in eight cases with ligation of the left coronary artery or its branches followed three months or longer and depicted in the literature. The electrocardiogram became normal in three patients, in all of whom there was no precordial lead, whereas it remained abnormal in five patients, in four of whom a precordial lead was taken. Q waves were present in the precordial lead in two patients. In another, a Q pattern occurred in the standard leads. The patterns in left and right ventricular wounds are seen to be more alike, as would be expected if the infarcted area was exerting a preponderant influence.

PRESENT STUDY

MATERIAL AND METHOD.—Electrocardiograms were obtained from twenty-three patients suffering from penetrating cardiac wounds. The number of tracings for each patient varied from one to twenty for each patient but was less than three in only three patients; the average number was seven. In two only the standard limb leads were taken; in five a single precordial lead (IV F) also was obtained on one or more occasions; in four the precordial Leads V_2, V_4, and V_6 were obtained in addition to the standard limb leads; in one there were three standard and six precordial leads (V_1-V_6); in eleven a total of twelve leads (three standard, V_1-V_6, and augmented unipolar leads from the extremities) were taken on one or more occasions. Of the twenty-one patients with one or more precordial leads, these were first recorded during the first week following the wound in six, during the second week in five, during the third week in four, and after this in the remaining six.

The first electrocardiogram was taken preoperatively in two patients, during the first day in six, during the second day in five, during the third day in six, during the fourth day in one, during the fifth day in two, and on the thirteenth day in one.

In nineteen patients the period of electrocardiographic study varied between eighteen days and three years. In five, this period was one month or less; in two, it terminated during the second month; in twelve it extended for three months or longer. Five patients in this last group had electrocardiograms over a period of from two to three years.

Eight patients were completely re-examined by me at periods varying between five and thirty-six months, averaging nineteen and one-half months, following the wound. Ten patients had follow-up roentgenologic studies.

The location of the wound was determined at operation in eighteen patients. In five it was in the right ventricle; in eleven, in the left ventricle; in one, in the left auricle; and in one it involved only the pericardium and a branch of the right pulmonary vein. In the five patients in whom operation was not performed, cardiac involvement was indicated in three by the presence of physical signs of cardiac tamponade, the fluoroscopic findings of an enlarged nonpulsating cardiac shadow, and the aspiration of blood from the pericardial sac. In the other two patients (Cases 19 and 20) these signs were not described, and the diagnosis of cardiac involvement was based chiefly on the electrocardiogram.

These cases are included in a study on the surgical aspects of penetrating cardiac wounds by Blau.[72]

FINDINGS.—

General Findings.—Table IV shows the evolution of the principal electrocardiographic changes and their interpretation in terms of the presence or absence of pericarditis, nonspecific myocardial damage, and localized myocardial damage resulting from the wound. The electrocardiograms returned to normal in six patients. The time of the normal tracing varied between ninety-five days and thirty-three months, averaging fifteen and one-half months. However, the time of the last preceding abnormal tracing averaged only forty-two days, indicating that there was usually a long period between these abnormal and the subsequent normal tracings. Therefore, these cases do not provide information as to the length of time actually required for the return to normal. Follow-up on the six patients with persistently abnormal electrocardiograms (Table V) was continued for an average period of twenty-one months, which is longer than the follow-up on the group of patients with a return to normal, so that it can be stated that the length of the follow-up period does not account for the differences between these two groups.

Definite evidences of pericarditis are present in seventeen patients. In seven of these (Cases 7, 9, 11, 16, 17, 22, and 23) no other abnormalities can be detected. Five others (Cases 5, 6, 14, 15, and 19) showed changes suggestive of pericarditis. The only one (Case 20) in whom no electrocardiographic evidence of pericarditis appeared is the patient in whom the first electrocardiogram was not taken until the thirteenth day, and the presence of anterior left ventricular damage makes it impossible to interpret the inversions of the T waves on any other basis, even though pericarditis may be a factor.

Patterns attributable to the wound and therefore of localizing value are definitely present in ten patients (Cases 1, 5, 6, 8, 10, 13, 14, 15, 19, and 20), questionably present in five (Cases 3, 4, 12, 18, 21), and absent in the remaining eight cases. There are ten patients (Cases 1, 2, 4, 6, 8, 9, 13, 14, 20 and 21) in whom, in addition to patterns of pericarditis and/or localized myocardial damage from the wound, various changes appeared which are classified as evidences of nonspecific myocardial damage. They include depression of the R-T segment in one or more leads (three cases), inversion of T waves during the first week in leads other than those reflecting the localized myocardial damage (three cases),

TABLE IV. EVOLUTION OF PRINCIPAL ELECTROCARDIOGRAPHIC FEATURES

CASE	LOCATION AND DESCRIPTION	PRE-OPERATIVE	FIRST DAY	2-7 DAYS	SECOND WEEK	THIRD WEEK	FOURTH WEEK	SECOND MONTH	THIRD MONTH	SUBSEQUENT	INTERPRETATION
1. E. R., 41-14906; 48 yr. C, M (Fig. 3)	R.V. (near apex, 2.0 cm.); stab			$R\text{-}T_{1,2}$, elev.; $R\text{-}T_3$, sl. dep.; $T_{1,2}$, diph.; T_3, neg.; aur. fibrill.; L.A.D.	$R\text{-}T_{1,2}$, iso.; $R\text{-}T_3$, sl. dep.; $T_{1,2}$, dome; T_3 neg.; sinus rhythm					*35th mo.:* L.A.D.; L.V.P.; def. i.v. cond. (inc. right B.B.B.); $T_{v3,5}$, diph.; T_{v4}, inv.; $S_{v4} > R_{v4}$; R.V. x-systoles	Early, pericarditis and myocardial damage; later, local damage R.V., from wound; nonspecific damage indicated by early diphasic $T_{1,2}$; aur. fibrill.
2. A. J. 43-760; 32 yr. C, M (Fig. 2)	R.V. (middle, 1.3 cm.); stab			$R\text{-}T_{1,2}$, elev.; $T_{1,2}$, diph.; T_3, neg.	$R\text{-}T_{1,2}$, elev.; $T_{1,2}$, up; T_3, sl. neg.	R-T's, iso.; T_1, $T_{v2,6}$, diph.; T_{v4}, neg. (v_4 taken over L.V.)	$T_{1,2,3}$, diph.; $T_{v2,4,6}$, neg.				Early, pericarditis and myocardial damage; later, pericarditis and ? local myocardial damage
3. L. J. 41-13661; 54 yr. C, M (Fig. 4)	R.V. (small); stab			$R\text{-}T_{1,2}$, elev.; $T_{1,2}$, up; T_3, neg.; occasional R.V. x-systole	$R\text{-}T_{1,2,3}$, iso.; T_1, diph.; $T_{2,3}$, neg.		T_1, T_{v6}, iso.; $T_{2,3}$, neg.; T_{v4}, diph. ($S_{v4} > R_{v4}$); T_{v2}, up	T_1, low up; $T_{2,3}$, neg.; $T_{v2,4,6}$, up		*95th day:* Normal ECG	Early, pericarditis; (later, pericarditis and ? T_2-T_3 pattern of R.V. damage
4. H. S., 41-17404; 30 yr. C, M	R.V. (upper); stab			$R\text{-}T_{1,2}$, elev.; $R\text{-}T_3$, sl. dep.; $T_{1,2}$, up, peaked; T_3, neg.; defective i.v. conduction		$R\text{-}T_{1,2,v6}$ sl. dep.; $R\text{-}T_{v2}$, elev.; $T_{1,2,v4,v6}$, neg. ($R_{v4} > S_{v4}$); T_3, low, up	R-T, iso.; T_2, diph.; $T_{1,v4,v6}$, neg.; QRS volt., lower, borderline in stand. leads			*33rd mo.:* normal ECG	Early, pericarditis, ? local subepicardial R.V. effect causing elev. $R\text{-}T_{v2}$ (4 mm.); early nonspecific myocardial damage (defective i.v. conduction)
5. G. G., 44-7450; 33 yr. C, M (Fig. 3)	R.V. (middle, large; near apex; smaller); stab			Incomplete right B.B.B.; low volt.; $R\text{-}T_{v3,v4}$, elev.; T_{v1}, neg.; $T_{v2,v4}$, diph.; $Q_{v1} = 5$ mm.							R.V. myocardial damage; ? localized pericarditis causing elev. $R\text{-}T_{v3,4}$

6. G. V., 41-13765; 29 yr. C, M (Fig. 5)	L.V. (near left coronary artery); stab		R-$T_{1,2}$, sl. elev.; T's, up; low volt.; small $Q_{2,3}$	R-$T_{1,2}$, sl. elev.; T's, low up; low volt.; small, $Q_{2,3}$	R-T, iso.; $T_{1,2}$, diph.; T_3, up; low volt. $Q_{2,3}$	$T_{1,2}$, sharply neg.; T_3, diph.; normal volt.; $Q_{2,3}$	$T_{1,2}$, neg.; T_3, up; prolonged QT; $Q_{2,3}$	$T_{1,2}$, neg.; T_3, up; $T_{v2,4,6}$, neg.; R_{v4}, less than 1 mm.; small $Q_{2,3}$		*36th mo.:* T_1, iso.; T_2, T_{v4}, diph.; $T_{v5,v6}$, neg.; diminished R_{v4}; low volt. stand. leads, $Q_{2,3}$, Q_{avf}	Early ECG's strongly suggestive of pericarditis; later, L.V. myocardial damage from wound, possibly infarction prolonged Q-T, a nonspecific change
7. C. D., 42-3530; 30 yr. C, M	L.V. (mid-anterior, small); stab			R-$T_{1,2}$, elev.; R-T_3, sl. dep.; $T_{1,2}$, up, peaked; T_3, neg.	R-$T_{1,2,3}$, iso.; $T_{1,2}$, diph.; T_3, up		R-$T_{1,2,v4,v6}$, elev.; R-T_3, sl. dep.; $T_{1,2,v6}$, up; $T_{3,v2,v4}$, diph.				ECG's show only pericarditis which recurred clinically at 30 days
8. G. E., 44-110; 33 yr. C, M (Fig. 6)	L.V. (bullet tunnelled lateral L.V. 3 cm. above apex)			R-$T_{1,2}$, elev.; T_1, up; T_2, diph.; T_3, neg.	R-T_1, sl. elev.; R-$T_{2,3}$, iso.; $T_{1,2}$, neg.; T_3, iso.; P-R = 0.22 sec.	R-T's, iso.; $T_{1,2}$, more deeply inv.; T_3, up; T_{v1-6}, neg.; P-R = 0.24 sec.	T waves all more deeply inv. except T_3 now, diph. and T_{v1}, up; P-R = 0.24 sec.	$T_{1,2,v3-6}$, neg.; T_3, diph.; $T_{v1,2}$, up; T invers. sl. less deep.; P-R = 0.20 sec.		*8th mo.:* T-wave invers. persistent though less marked in $_{1,2,v3-6}$; P-R = 0.24 sec.	Early, pericarditis; later (18 days and subsequent), L.V. myocardial damage; nonspecific myocardial damage
9. O. H., X-6627; 40 yr. C, F	L.V. (3.0 cm. above apex); stab		S-$T_{1,2}$, elev.; S-T_3, iso.; $T_{1,2}$, up; T_3, neg.; low volt.	Same as 1st day except greater S-T elev., incr. volt., parox. aur. fibrill.							Early stage of pericarditis; died seventh day, autopsy: purulent pericarditis, nonspecific damage indicated by auricular fibrillation
10. E. W. 42-5620; 33 yr. C, M (Fig. 6)	L.V. (1.75 cm. long); stab			R-$T_{1,2}$, elev.; R-T_3, iso.; $T_{1,2}$, up; T_3, iso.; L.A.D.		R-$T_{1,2,3}$, iso.; convex; $T_{1,2,3}$, neg.		$T_{1,2,3,v6}$, neg.; L.A.D. with S_3 varying with respiration		*28th mo.:* T_1, T_{v5}, diph.; T_2, T_{v6}, neg.; L.A.D.	Early, pericarditis; left ventricular damage at twenty-eighth month

Aur. fibrill., auricular fibrillation; A-V, auriculoventricular; B.B.B., bundle branch block; C, colored; def. i.v. cond., defective intraventricular conduction; dep., depressed; diph., diphasic; elev., elevated; F, female; inc., incomplete; incr., increased; inv., inverted; invers., inversion; iso., isoelectric; i.v., intraventricular; L.A., left auricle; L.A.D., left axis deviation; L.V., left ventricle; L.V.P., left ventricular preponderance; M, male; Mo., month; neg., negative; parox. aur. fibrill., paroxysmal auricular fibrillation; p.o., postoperative; Q_{AVF}, Q wave in augmented unipolar lead from left leg; R-T, R-I or RS-T segment; R.V., right ventricular; sl., slightly; S > R, S exceeds R in amplitude; stand., standard; S-T, R-T or RS-T segment; T's, T waves; volt., voltage; W, white; x-systoles, extra- or premature systoles.

TABLE IV. EVOLUTION OF PRINCIPAL ELECTROCARDIOGRAPHIC FEATURES—CONT'D

CASE	LOCATION AND DESCRIPTION	PREOPERATIVE	FIRST DAY	2-7 DAYS	SECOND WEEK	THIRD WEEK	FOURTH WEEK	SECOND MONTH	THIRD MONTH	SUBSEQUENT	INTERPRETATION
11. B. Q. X-17261; 26 yr. C, M	L.V. (1.0 cm. to left of left coronary artery; 1.0 cm. below A-V junction); stab	R-$T_{1,2,3}$, iso.; $T_{1,2}$, up; T_3, diph.; basilar notch; $QRS_{1,2,3}$	*8 hours p.o.:* R-T_1, elev.; T_1, tall, peaked; L.A.D. *24 hours:* R-$T_{1,2}$, elev.; $T_{1,2}$, tall, peaked; QRS volt. lower; L.A.D.	R-T_1, iso.; R-T_2, elev.; $T_{1,2,3}$, up; low volt.; L.A.D.	R-$T_{1,2,3}$, iso.; $T_{1,2,3}$, up; low volt.; L.A.D.	$T_{1,2,3,4f}$, low and dome shaped; low volt.; L.A.D.	T's same; QRS volt. incr. to normal; L.A.D.				Only pericarditis
12. L. G., 41-568; 21 yr. W, M (Fig. 2)	L.V. (Transverse, at junction with L.A.); stab			R-$T_{1,2,3}$, elev.; $T_{1,2}$, up, peaked; T_3, up; small $Q_{1,2,3}$	R-$T_{1,2,4f}$, elev.; T's, up; small $Q_{1,2,4f}$	R-T's, iso.; $T_{1,4}$, diph.; $T_{2,3}$, up; small $Q_{1,2,4f}$	$T_{1,2,4f}$, neg.; T_3, iso.; small $Q_{1,2,3,4f}$	*31 days:* $T_{1,2,3}$, low up; T_4, diph. *45 days:* $T_{1,4}$, neg.; $T_{2,3}$, up; Q's as before		*30th mo.:* Normal ECG (small $Q_{1,2,3,v4,5,6}$)	Pericarditis; ? "T_1 pattern" of L.V. injury at 45 days; Q's insignificant; ECG signs of recurrent pericarditis at 31 days
13. G. C., 43-15498; 33 yr. C, M	L.V. (2.0 cm., anterior, near base); stab			R-T_1, sl. elev.; R-$T_{2,3}$, iso.; $T_{1,2}$, up, peaked; T_3, neg.; L.A.D.; borderline volt	R-$T_{1,v4-6}$, sl. dep.; R-T_3, sl. elev.; R-$T_{2,v2,3}$, iso.; $T_{1,2,v1-6}$, diph.; semi-horizontal position; L.A.D.; borderline volt	R-T_1, sl. dep.; R-T_2, iso.; R-T_3, sl. elev.; $T_{1,2}$, diph.; T_3, neg.; L.A.D.; borderline volt				*3½ mo.:* $T_{1,2,v6}$, low up; T_3, diph.; $T_{v2,4}$, up; normal volt.; L.A.D. *11 mo.:* Normal ECG (12 leads); horizontal position of heart; L.A.D.	Pericarditis; diffuse myocardial damage (second week); L.V. myocardial damage (3½ months)

14. D. B., 42-17093; 19 yr. W, M (Fig. 6)	L.V. (2.0 cm.); stab			R-$T_{1,2,3}$, iso.; T_1, diph.; $T_{2,3}$, neg.; Q_3, varying with respiration	As on second day except rate slower			R-$T_{1,v4,6}$, sl. dep.; $T_{1,2,v2,4,6}$, neg.; (Lead III artefact)		*93rd day:* R-T's, iso.; arched in $_{1,v4,6}$; $T_{1,v4,6}$, neg.; T_2, diph.; T_3, T_{v2}, up; Q_3 varies from 2-4 mm. with respiration *21st mo.:* $T_{1,2,v5,6}$, diph.; T_{v4}, low, double; Q_3 varies 6-7 mm.; intermediate position	Probable pericarditis (negative T's, 51 days); L.V. damage (all ECG's); Q_3 probably postural (recumbent ECG at twenty-first month shows semivertical heart Q_3 = 2-3 mm.; no Q_{avf}); nonspecific damage indicated by early inversion $T_{2,3}$
15. S. J., V-13385; 44 yr. C, M (Fig. 5)	L.V. (with division left coronary artery); stab	R-$T_{1,2,4f}$, elev.; T's, up; small $Q_{1,2,3}$; R_{4f}, absent; low volt.									Anterior infarction plus ? hemopericardium
16. C. H., 43-2952; 43 yr. C, M	L.V. (2 small wounds anteriorly); stab			R-$T_{1,2}$, elev.; R-T_3, iso.; $T_{1,2}$, up, peaked; T_3, iso.; L.A.D.							Pericarditis only

TABLE IV. EVOLUTION OF PRINCIPAL ELECTROCARDIOGRAPHIC FEATURES—CONT'D

CASE	LOCATION AND DESCRIPTION	PRE-OPERATIVE	FIRST DAY	2-7 DAYS	SECOND WEEK	THIRD WEEK	FOUETH WEEK	SECOND MONTH	THIRD MONTH	SUBSEQUENT	INTERPRETATION
17. O. P., 41-1032; 23 yr. C, M (Fig. 1)	Pulmonary vein and pericardium		*Immediate p.o.:* R-$T_{1,2,3}$, iso.; T_1, low, up; $T_{2,3}$, up; L.A.D. *22 hours:* R-$T_{1,2,3}$, elev.; $T_{1,2}$, up, peaked; T_3, neg.; QRS, volt. lower; L.A.D.	R-$T_{1,2}$, elev.; R-T_3, dep.; $T_{1,2}$, up; T_3, neg.; L.A.D.	R-$T_{1,2}$, sl. elev.; R-T_3, iso.; T's as before	R-T's, iso.; arched in $_{1,2,4f}$, $T_{1,2,4}$, neg.	$T_{1,2,4f}$, neg.		$T_{1,2}$, sl. neg.; T_3, low up	*97 days:* R-$T_{1,2,3}$, elev.; R-T_{4f}, ? dep.; $T_{1,2,3}$, up; T_{4f}, ? neg.	Pericarditis persistent at 76 days; recurrent acute at 97 days
18. H. P., V-5186; 23 yr. C, M (Fig. 1)	Left atrium (2.5 cm.); stab		R-$T_{1,2}$, elev.; R-T_3, sl. dep.; $T_{1,2,3}$, up; borderline volt.; $P_{1,2}$, sl. notch, small	R-$T_{1,2,4f}$, elev.; R-T_3, iso.; $T_{1,2,4}$, low up; L.A.D., with variable Q_3; normal volt.; $P_{1,2}$, sl. notch, small	R-$T_{1,2,4f}$, elev.; $T_{1,2,3}$, low up; T_{4f}, notched; L.A.D. gone; $P_{1,2}$, sl. notch, small	R-$T_{1,2,4}$, dep.; $T_{1,2,4}$, neg.; sl. L.A.D., Q_3; $P_{1,2}$, sl. notch; normal volt.	R-$T_{1,2,4}$, sl. dep.; $T_{1,2,4}$, neg.; deeper; L.A.D. gone; $P_{1,2}$, sl. notch, lower, duration, approx. 0.11 sec.				Pericarditis; suggestion of atrial damage (left)
19. O. P., 42-15355; 26 yr. C, M (Fig. 7)	? Stabbed in back with long knife			R-T_1, sl. elev.; R-$T_{2,3,v2,4,6}$, iso.; $T_{1,2,3,v6}$, neg.; $Q_{1,v6}$, small; $Q_{2,3}$, larger	R-T's, iso.; T_1, low up; $T_{2,3,v6}$, neg.; Q waves as before	T_1, taller; $T_{2,3}$, deeper; T_{v6}, neg.; $Q_{2,3}$, deeper		T_1, normal; $T_{2,3}$, deeper; $T_{v2,4}$, tall; T_{v6}, up; small $Q_{1,v6}$, deep $Q_{2,3}$			Probable pericarditis; myocardial damage posterior—basal L.V.; ? wound or infarction from laceration right coronary

20. P. E., X-11784; 27 yr. C, M (Fig. 7)	? Precordial wound 5.0 cm. left third interspace, nipple line; stab				R-T_1, sl. dep.; R-$T_{1,2,4f}$, arched; $T_{1,2,4f}$, neg.; T_3, up; L.A.D. R_{4f}, absent	Same as second week	T_1, less deep; T_{4f}, deeper; $T_{2,3}$, neg.; R_{4f}, absent	Same as fourth week			L.V. myocardial damage; ? wound or infarction from laceration left coronary artery
21. L. Mc., 44-4951; 32 yr. C, F (Fig. 7)	? Several puncture wounds on chest wall from icepick; stab		R-$T_{1,2}$, sl. dep; $T_{1,v4,v6}$, up; $T_{2,v2}$, up, double; T_3, neg.	R-$T_{1,2}$, sl. dep.; R-$T_{v1,2}$, sl. elev.; T_{v1}, diph.	R-T elev. all leads except lead III; $T_{1,2,v2-6}$, up and peaked; T_{v1}, diph.					*5 mo.:* R-$T_{1,2,3,v6}$, iso.; R-T_{v1-5}, elev. (high volt.); all T's up except T_3; L.A.D.; semi-horizontal heart; ECG within normal limits	Pericarditis (second week): Suggestion of R.V. damage (R-T and T changes in $_{v1}$; R-T changes $_{v2}$); nonspecific damage indicated by R-T depression in early tracings
22. E. A., 44-1421; 46 yr. C, M	? Lower sternum just left midline; stab		*7 hours:* R-T, iso., except R-T_{v3} elev.; T's, up except $_{v6}$, low up	R-T $_{1,2,v4-6}$, elev.; T's up except T_3		R-T's iso.; $T_{1,2,3,v4-6}$, neg.					Pericarditis; no definite myocardial damage
23. M. O., 43-14165; 29 yr. C, F	? Wound left second interspace, 7.5 cm. from midsternal line; stab			R-$T_{1,2,3}$, elev.; T's, up; low volt.; L.A.D.	R-T's, iso.; $T_{1,2,3}$, low, dome.; low volt.; normal axis					*11 mo.:* ECG within normal limits (borderline volt)	Pericarditis only

TABLE V. LATE ELECTROCARDIOGRAPHIC FINDINGS AMONG TWELVE PATIENTS WITH CARDIAC WOUNDS

CASE	NUMBER OF LEADS	TYPE OF FINDING	TIME OF FOLLOW-UP (MONTHS)	NUMBER OF PATIENTS
		A. Left Ventricular Wounds (Six Cases)		
13, 12 (Fig. 2)	12, 9	Normal electrocardiogram	11, 30	2
8 (Fig. 6)	12	Inverted T_1, T_2, T_{V3-6}; P-R = 0.24 sec.	8	1
14 (Fig. 6)	12	Diphasic $T_{1,2,V5,6}$; T_{V4} low up	21	1
10 (Fig. 6)	12	Diphasic $T_1 + T_{V5}$; inverted $T_2 + T_{V6}$	28	1
*6 (Fig. 5)	12	Inverted $T_{V5} + T_{V6}$; diphasic $T_2 + T_{V4}$; isoelectric T_1; low voltage; diminished R_{V4}	36	1
13	12	Low voltage of T_1, T_2, + T_{V6}	3½	—
		B. Right Ventricular Wounds (Three Cases)		
3, 4 (Fig. 4)	6, 12	Normal electrocardiogram	3, 33	2
1 (Fig. 3)	12	Defective intraventricular conduction (incomplete right bundle branch block), right ventricular premature systoles; diphasic T_{V3}, T_{V5}; inverted T_{V4} ($S_{V4} > R_{V4}$), left ventricular preponderance	35	1
		C. Pulmonary Vein and Pericardium (One Case)		
17 (Fig. 1)	4	Elevated S-$T_{1,2,3}$ (recurrent pericarditis)	3	1
		D. Unknown Location (Two Cases)		
21 (Fig. 7), 23	12, 12	Normal electrocardiogram	5, 11	2
		E. Total Cases (Twelve)		
		Normal electrocardiogram	15.5 (Av.)	6
		Abnormal electrocardiogram	21.9 (Av.)	6

$S_{V4} > R_{V4}$ = S wave in V_4 exceeds R wave in V_4 in amplitude.
*Probable complicating anterior infarction.

auricular fibrillation (two cases), prolonged Q-T interval (one case), defective intraventricular conduction (one case), and prolonged auriculoventricular conduction (one case).

Pericarditis.—The evolution of the electrocardiographic effects of pericarditis is best considered in chronologic order since it follows a fairly regular course and since it is important to know what to expect at a particular stage.

RS-T Segment Patterns: Of the two tracings taken preoperatively (Cases 11, 15—Fig. 5), the first is within normal limits and the second shows the pattern of acute anterior myocardial infarction in which it is impossible to distinguish with certainty changes which may be due to the associated hemopericardium. There are eight patients with electrocardiograms taken preoperatively and/or during the first twenty-four hours. In the first patient, just mentioned (Case 11), with an essentially normal preoperative tracing, an electrocardiogram taken eight hours after the operation shows the characteristic changes of pericarditis. The findings in the second (Case 15) have been described. In a third patient (Case 17—Fig. 1), a tracing taken immediately postoperatively showed nonspecific abnormalities but twenty-two hours later is suggestive of acute pericarditis. Of the remaining five patients, two show definite pericarditis (Cases 9, 18—Fig. 1), one suggestive changes (Case 6), and two only nonspecific abnormalities (Cases 21, 22). Thus, in five of these eight patients, the electrocardiogram taken during the first day shows pericarditis as early as eight hours postoperatively.

By the second day and thereafter during the first two or three weeks, the characteristic upwardly concave elevations of the RS-T segments were almost uniformly present. Of the standard leads they involved Leads I and II most frequently and were present in Lead III also in only one patient. In three patients this segment was slightly depressed in Lead III. In the fourteen patients in whom there are sufficient tracings at this stage for analysis of changes of the RS-T segment, elevations disappear in from eight to eighteen days, averaging thirteen days (Figs. 1 and 2). Such elevation appears first in one or more of the precordial leads in three of the five cases suitable for determining this point. Ten patients have electrocardiograms with one or more precordial leads taken at the same time or within a few days of the time when this segment became isoelectric in the standard leads. In seven, the RS-T elevation in the precordial leads disappears simultaneously, while in the other three it persists for a longer time in the precordial leads. It is more striking in the precordial leads in eight of eleven cases suitable for comparison. In general, however, since the RS-T changes are easily visible in the standard leads in the great majority of cases, the precordial leads are only occasionally of additional help as far as this feature is concerned. In two patients RS-T elevation recurred. In one, this accompanied definite clinical signs of pericarditis. In the other, no pericardial findings were elicited, but the patient suffered from thoracic empyema which necessitated surgical drainage (Case 17—Fig. 1).

T-Wave Patterns: Abnormalities of the T waves during the days and weeks following a penetrating cardiac wound may be due to pericarditis, to the wound itself, or to nonspecific types of myocardial damage from shock, anemia, or other less frequent causes. The presence of these multiple factors might appear to make it impossible to ascribe a particular T-wave abnormality specifically to pericarditis. Nevertheless, from a consideration of the behavior of the T waves in uncomplicated pericarditis of other types, it is possible to distinguish certain trends of influence upon the T waves of the pericardial factor in the present series of patients. In various types of pericarditis and in the present patients the

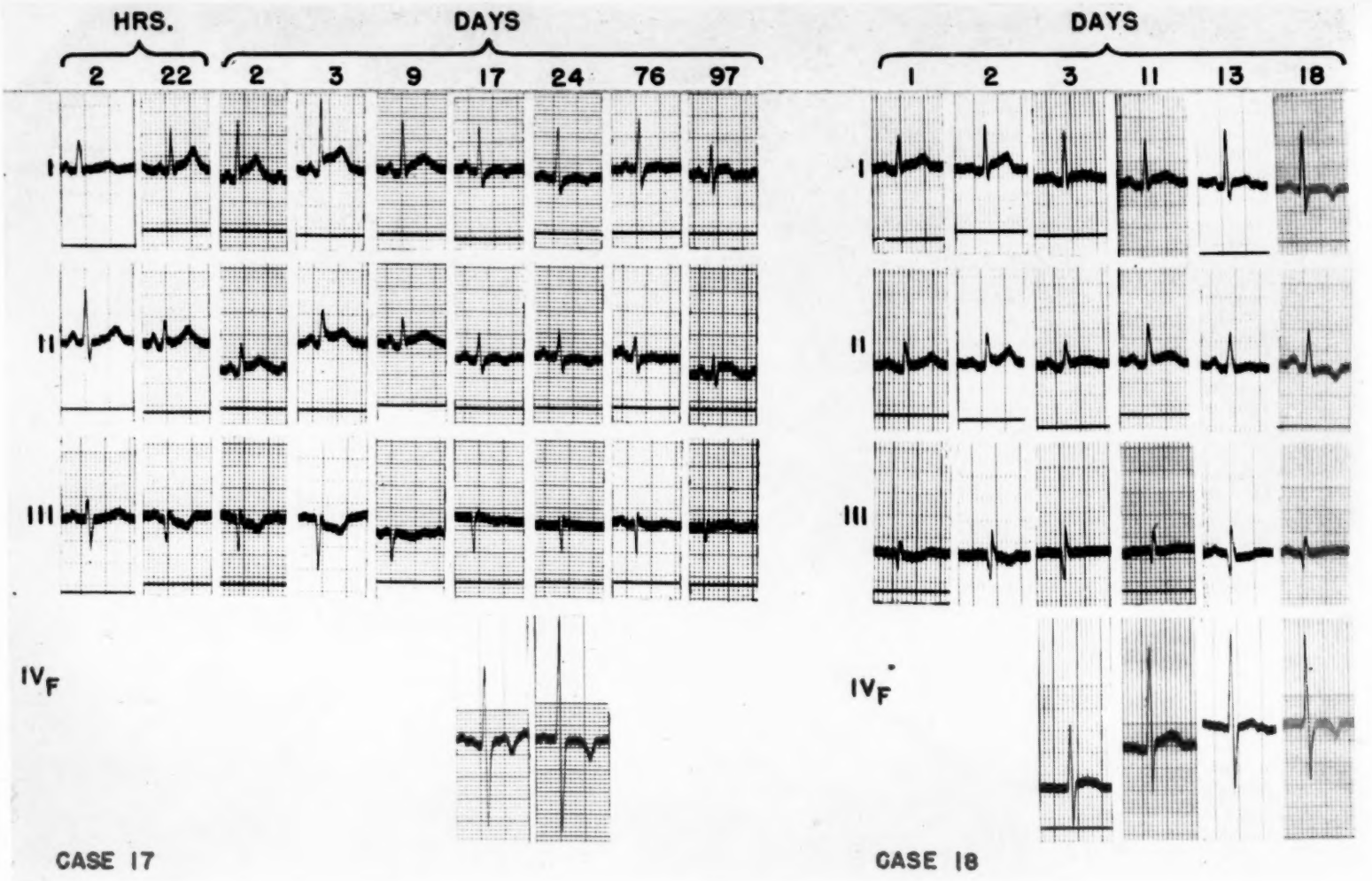

Fig. 1.—Electrocardiograms in two cases without ventricular wounds illustrating characteristic patterns of pericarditis.

Case 17. Stab wound of pericardium and pulmonary vein; myocardium intact. Empyema drained at three months. Note (a) appearance of effects of pericarditis at twenty-two hours; (b) return of R-T segment to isoelectric level and appearance of inverted T waves at seventeen days; (c) persistence of T-wave inversion at seventy-six days; (d) recurrence of R-T elevations at ninety-seven days (recurrent acute pericarditis).

Case 18. Stab wound, left atrium. Note (a) early R-T elevation on first day; (b) classical pericarditis on second day; (c) slight notching of $P_1 + P_2$, suggesting left atrial damage; (d) return of R-T to isoelectric with diphasic T_1, $_2$, $_3$ on thirteenth day; (e) cove-plane T-wave inversions on eighteenth day. Note resemblance

T waves are frequently tall and peaked during the first part of the early period when RS-T elevation is present. These peaks tend to round off within a few days, but inversion nearly always occurs later, after the RS-T elevation has disappeared at the end of the second week or the early part of the third week

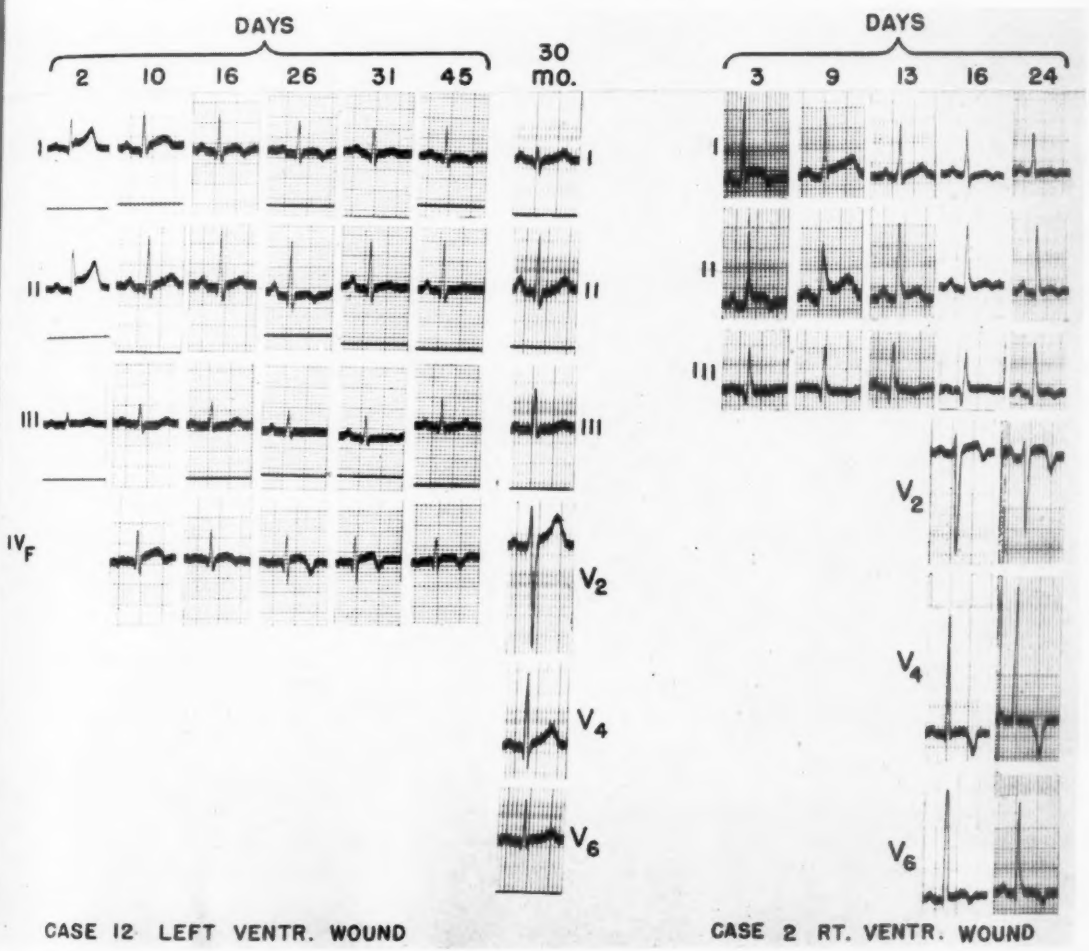

Fig. 2.—Electrocardiograms in right and left ventricular wounds illustrating preponderant influence of pericarditis.

Case 12. Stab wound of left ventricle. Note (a) recurrent acute pericarditis at thirty-one days with reversal of T-wave direction in standard leads; (b) so-called "late T_1 pattern" at forty-five days; (c) normal electrocardiogram at thirty months.

Case 2. Stab wound of right ventricle. Note (a) diphasic $T_{1, 2}$ at three days, suggesting nonspecific myocardial damage; (b) lack of localizing pattern, with inversion of T waves in all leads, characteristic of pericarditis, at twenty-four days.

(see Figs. 1 and 2). In the present series the tracings of only six of twenty-one patients with electrocardiograms taken during the first week show diphasic or inverted T waves in leads other than III or V_1, whereas these changes are present in twelve of thirteen patients with tracings taken during the third week. Among

ten patients with frequent electrocardiograms, inversions of T waves appear between the eleventh and nineteenth days, averaging sixteen days. Their presence during the first week is associated with clinical or other electrocardiographic evidences of myocardial damage (Cases 1, 2, 5, 8, 14, and 19).

A second consideration relating the abnormalities of the T waves to pericarditis is the tendency in various types of generalized pericarditis toward widespread, more or less persistent inversions of T waves. Of the present cases suitable for analysis of this point, diphasic or inverted T waves are present in each of the standard leads from the extremities in eight of fifteen cases and in each precordial lead in five of ten cases. Thus in many cases the wide distribution seems to exclude localized myocardial damage, and the persistence and depth of these inversions excludes nonspecific types of myocardial damage as the sole or most important causes.

A third consideration is the presence in two patients (Fig. 1), without wounds of the ventricles, of abnormalities of the T waves closely similar in the time of their appearance, contour, and distribution to those seen in patients with wounds of either ventricle (Fig. 2). Since the wounds did not involve the ventricles, they cannot explain directly the abnormalities of the T waves. Nonspecific ventricular myocardial damage incident to shock, anemia, or displacement of the heart would not be as persistent. Exactly comparable changes are present in many cases of uncomplicated pericarditis of varied etiology. Therefore, pericarditis is the chief cause of these abnormalities in these two patients. The similarity of the pattern to that seen in wounds of either ventricle (compare Figs. 1 and 2) indicates the importance of pericarditis as a factor in the production of the electrocardiographic findings in ventricular wounds.

Low voltage of the QRS complexes of the standard leads from the extremities is present in six patients. This change is consistent with, though not pathognomonic of, pericarditis.

Localizing Findings.—

Right Ventricular Wounds: Five patients (Cases 1 to 5) were found at operation to have wounds of the right ventricle. The electrocardiograms of two patients show definite evidences of localized right ventricular myocardial damage as illustrated in Fig. 3 and described in the legend. One factor complicating the interpretation in Case 5 is the presence at autopsy of chronic rheumatic heart disease with mitral stenosis and insufficiency and right ventricular hypertrophy. However, the heart weighed only 410 grams and there was a small hemorrhagic extravasation in the interventricular septum which, along with the wounds of the right ventricle, seems to be a better explanation of the right bundle branch block. Furthermore, right ventricular hypertrophy would not explain the R-T segment elevations which are most marked in the precordial leads over the right ventricle. In one patient (Case 1) there was coincidental asymptomatic hypertensive cardiovascular disease with moderate left ventricular hypertrophy and probably also syphilitic aortitis. However, localized myocardial damage as indicated by the T-wave changes in Lead V_3-V_5 which are not present in Lead V_6

would be very unusual in either of these two conditions. Also, the equal amplitude of the R and S waves in Lead V_4 indicate that the precordial electrode was near the interventricular septum. This corresponds with the location of the wound in the right ventricle near the septum.

Two additional patients in this group have questionable localizing findings. Pertinent tracings are shown in Fig. 4. Case 3 with a "T_2, T_3 pattern" is considered questionable because of the fact that pericarditis may cause inversions of T waves at this time and in these leads alone (vide infra). However, the number of reported cases of right ventricular wounds with persistence of this pattern beyond a three-month period indicates that this may be valid as a localizing

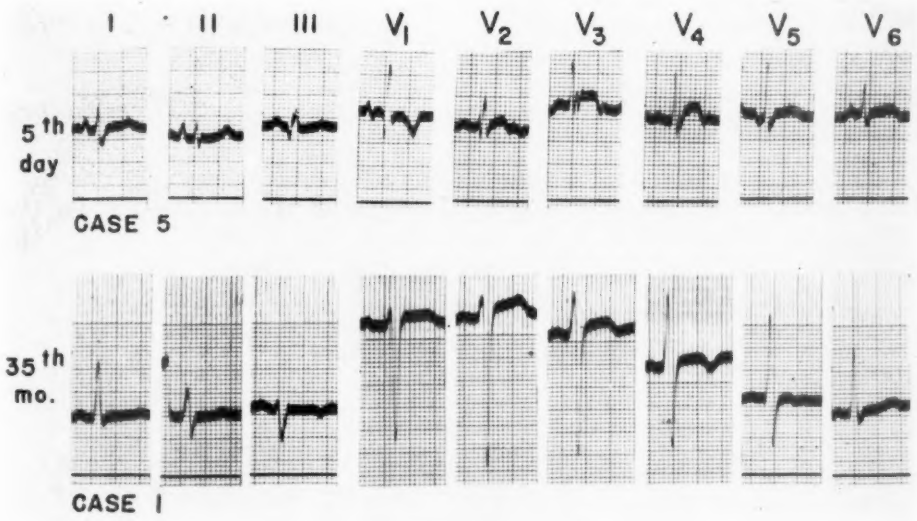

Fig. 3.—Definite localizing patterns in right ventricular wounds.
Case 5. Incomplete right bundle branch block; elevation R-$T_{V3, 4}$, indicating localized subepicardial process.
Case 1. Note (a) late localized T-wave changes in V_3-V_5 corresponding to location of wound at left border of right ventricle; (b) incomplete right bundle branch block; (c) left ventricular preponderance due to associated hypertensive cardiovascular disease.

pattern in some instances. The evidence of localized damage in Case 4 is admittedly slender, and the observed elevations of the R-T segments in Lead V_2 on the fifteenth day could be dependent upon the high voltage of the QRS complex. However, they do suggest a localized subepicardial process. In the final patient (Case 2—Fig. 2), the electrocardiographic abnormalities are attributable to pericarditis.

Left Ventricular Wounds: There are eleven patients in whom left ventricular wounds were discovered at operation. In six definite electrocardiographic findings of left ventricular damage thought to be due to the wound are present. Electrocardiograms in two of these patients with known or probable injury to the left coronary artery are shown in Fig. 5. It is possible that in the second (Case 6) the diminished R waves are due to the wound itself. However, if this

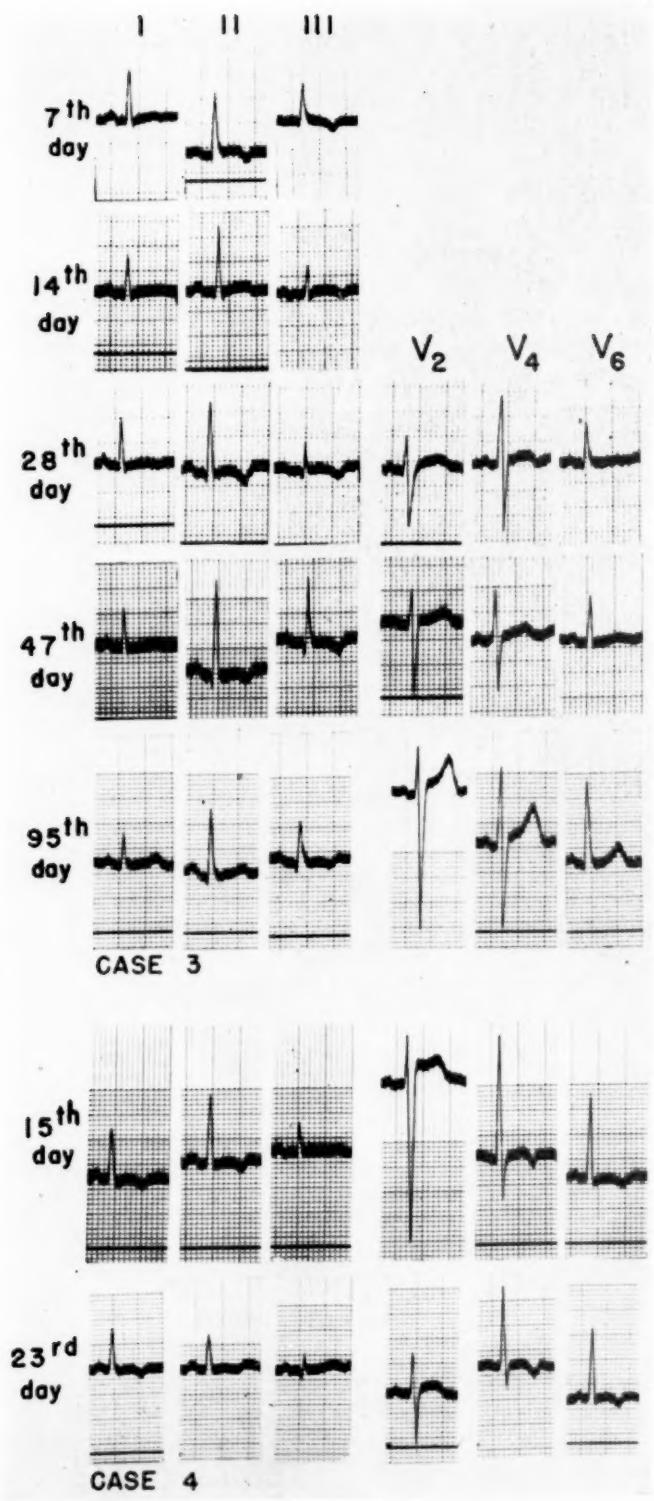

Fig. 4.—*For legend, see opposite page.*

were so, one would expect Q patterns or their equivalents in more of the cases with multiple precordial leads. The infrequency of this finding as well as the fact that the wound was very close to the left coronary artery makes it probable that this vessel was occluded, resulting in an anteroapical myocardial infarct. In both of these cases the pattern of anterior infarction gives indirect evidence of the location of the wound in the region of the left coronary artery.

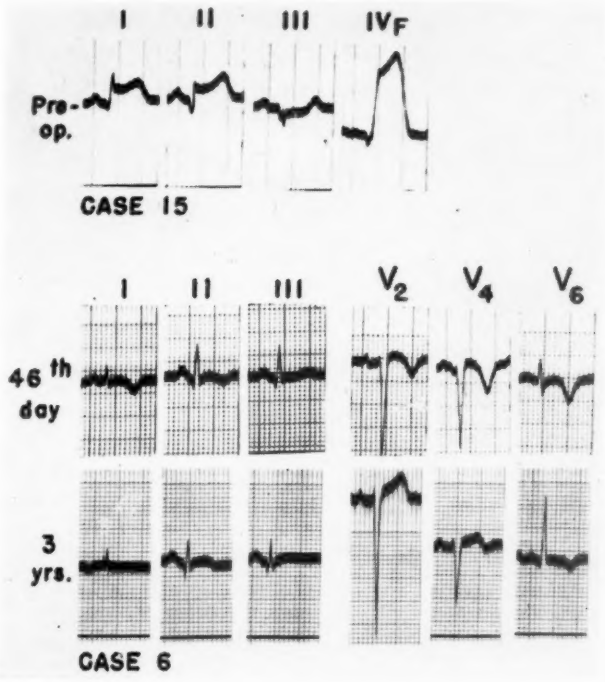

Fig. 5.—Left ventricular wounds with known or probable injury to left coronary artery.

Case 15. Patient found to have laceration of left ventricle dividing descending branch of left coronary artery. Note Q pattern, marked R-T elevation characteristic of recent anterior infarct. Unusual degree of elevation probably partly due to hemopericardium.

Case 6. Wound 3 to 4 mm. from left coronary artery; attempt made to avoid its suture. Note (a) very small R waves in V_4 probably due to anterior infarction, possibly to wound itself; (b) regression of T-wave inversions, persistently small R waves at three years.

Four of the six patients with left ventricular wounds with definite localizing findings have T-wave changes in Leads I and II and in the precordial leads over the left ventricle. Fig. 6 illustrates three such cases. Each of these young men was re-examined completely by me at the time of the last recorded electrocardiogram, and hypertension, valvular lesions, and left ventricular enlargement were excluded. Furthermore, the precordial leads do not show left ventricular hyper-

Fig. 4.—Right ventricular wounds with questionable localizing signs.

Case 3. Note preponderant inversion of $T_{2,3}$ persisting through the forty-seventh day, the so-called "T_2, T_3 pattern."

Case 4. Note (a) isolated elevation of R-T segment in V_2 on fifteenth and twenty-third day, suggesting localized subepicardial process in right ventricle; (b) presence of so-called "late T_1" pattern on twenty-third day, here associated with a right instead of a left ventricular wound and probably due to subacute stage of pericarditis.

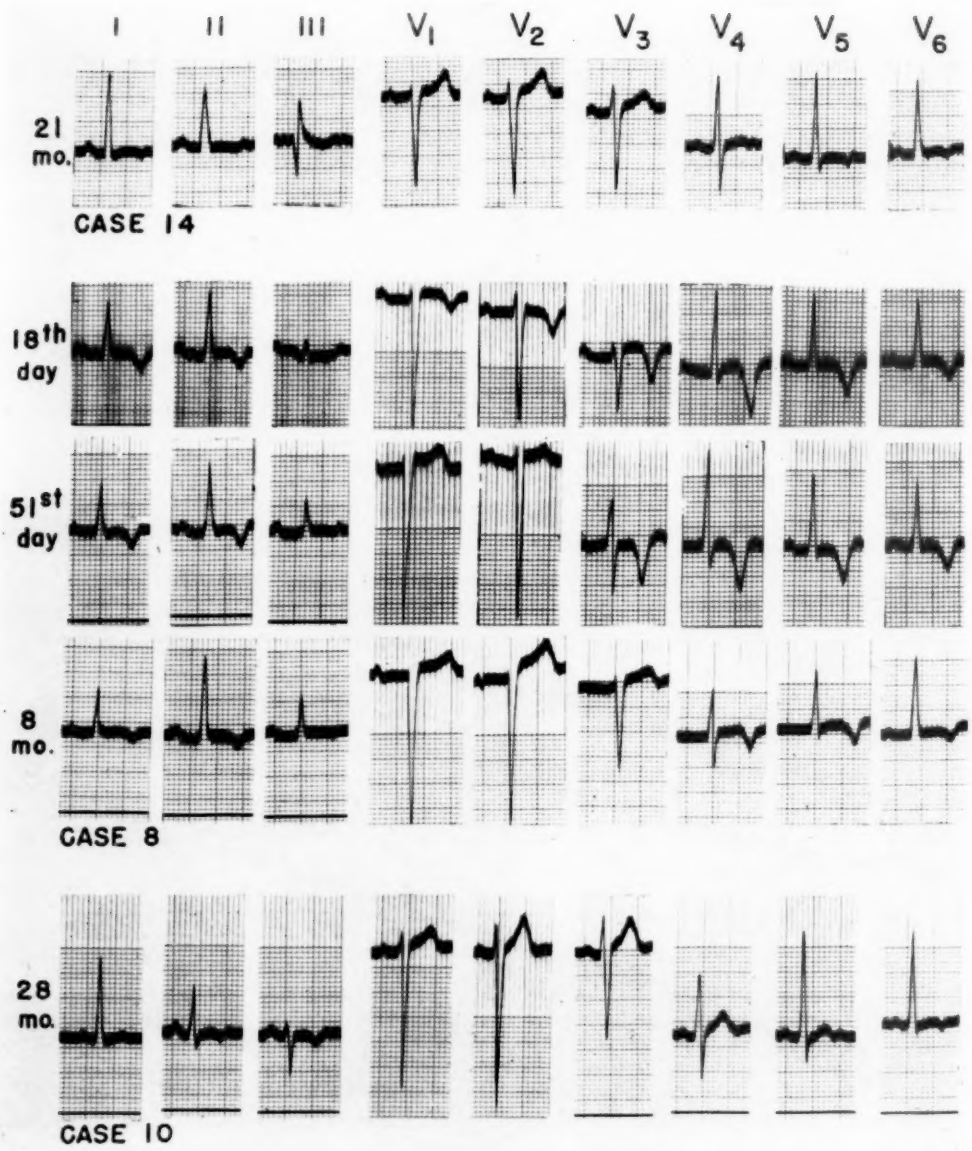

Fig. 6.—Left ventricular wounds with localizing T-wave patterns.

Case 14. Inverted T waves in Leads I, II, $V_5 + V_6$. Q_3 postural (see Table IV). [Inverted T waves previously present in V_2 and V_4 at fifty-one days and in V_4 at ninety-three days (not shown) have disappeared, probably indicating decrease in size of damaged area, localization in anterolateral left ventricle.] Cardiovascular examination otherwise negative at twenty-one months.

Case 8. Note (a) deep T waves in V_3-V_6 on eighteenth day, the depth and contour suggesting myocardial damage rather than pericarditis alone; (b) decreased height of R wave in V_3 on eighteenth day, suggesting involvement of almost entire thickness of ventricular wall at this point; (c) persistent prolonged A-V conduction. Cardiovascular examination normal at eight months except wide splitting of first cardiac sound.

Case 10. Persistent lateral left ventricular damage at twenty-eight months in absence of symptoms and physical or roentgen abnormalities.

trophy, since the time intervals from the initial QRS deflections to the peak of the R waves are 0.04 second or less in the leads over the left ventricle. For these reasons it may be assumed safely that coincidental cardiac disease is not a factor. Inspection of Table IV reveals that T-wave inversions in Cases 10 and 14 were present also in a number of earlier tracings during the first and second months. The difficulty in interpreting these earlier T-wave changes as due to localized left ventricular injury is shown by the fact that each of the three patients with right ventricular wounds (including Case 2—Fig. 2, and Case 4—Fig. 4) with tracings during this intermediate period showed abnormalities in the same leads.

When the T waves are as deep at any time as those in Case 8 of Fig. 6, localized damage may be assumed to be present since pericarditis alone rarely produces such T waves. The T-wave inversions occurring during the first week may indicate localized ventricular injury since pericarditis rarely causes inversions at this time, particularly if elevation of the R-T segment is present concurrently. However, nonspecific types of myocardial damage incident to shock, anemia, or the operative procedure may produce similar changes during this period, and so, again, it is unsafe to consider them as localizing findings.

The same considerations regarding the persistence of effects of pericarditis apply to the significance of the disappearance of abnormalities of the T waves in certain precordial leads while they are still present in others (see Case 6—Fig. 5). This may be due to the subsidence of the generalized pericarditis and perhaps should be so considered in most cases with tracings during the first two or three months. However, it is probable that in some of these tracings this represents a diminution in the size of the injured area. When it is large, it may affect the T waves in leads taken over the opposite ventricle, as is commonly seen in leads over the right ventricle in instances of anteroseptal infarcts of the left ventricle due to coronary heart disease.

Case 12 (Fig. 2) is considered to show questionable localizing findings since the last abnormal electrocardiogram showing limitation of T-wave abnormalities to Leads I and IVF is taken at forty-five days, during a period when pericarditis could still be exerting its effects. Of the four patients without localizing changes, two (Cases 9 and 16) had only one or a few electrocardiograms, and these were taken during the first week, and the other two (Cases 7 and 11) had tracings only during the first month. All showed typical changes of pericarditis.

Wounds Not Involving the Ventricles: The electrocardiograms of the two patients with wounds not involving the ventricles are shown in Fig. 1. In a patient with a left auricular wound (Case 18), the only localizing finding is notching of the P waves in Leads I and II. This is considered to be of questionable localizing significance because it is not marked enough to be definitely abnormal.

Wounds in Patients Without Operation: Two of the five patients have electrocardiograms with definite localizing findings (Cases 19 and 20—Fig. 7). Both T and Q patterns are present. The presence of Q waves raises the question of whether the coronary arteries were involved in the lacerations. In Case 19 the existence of a cardiac wound was not suspected until the electrocardiogram

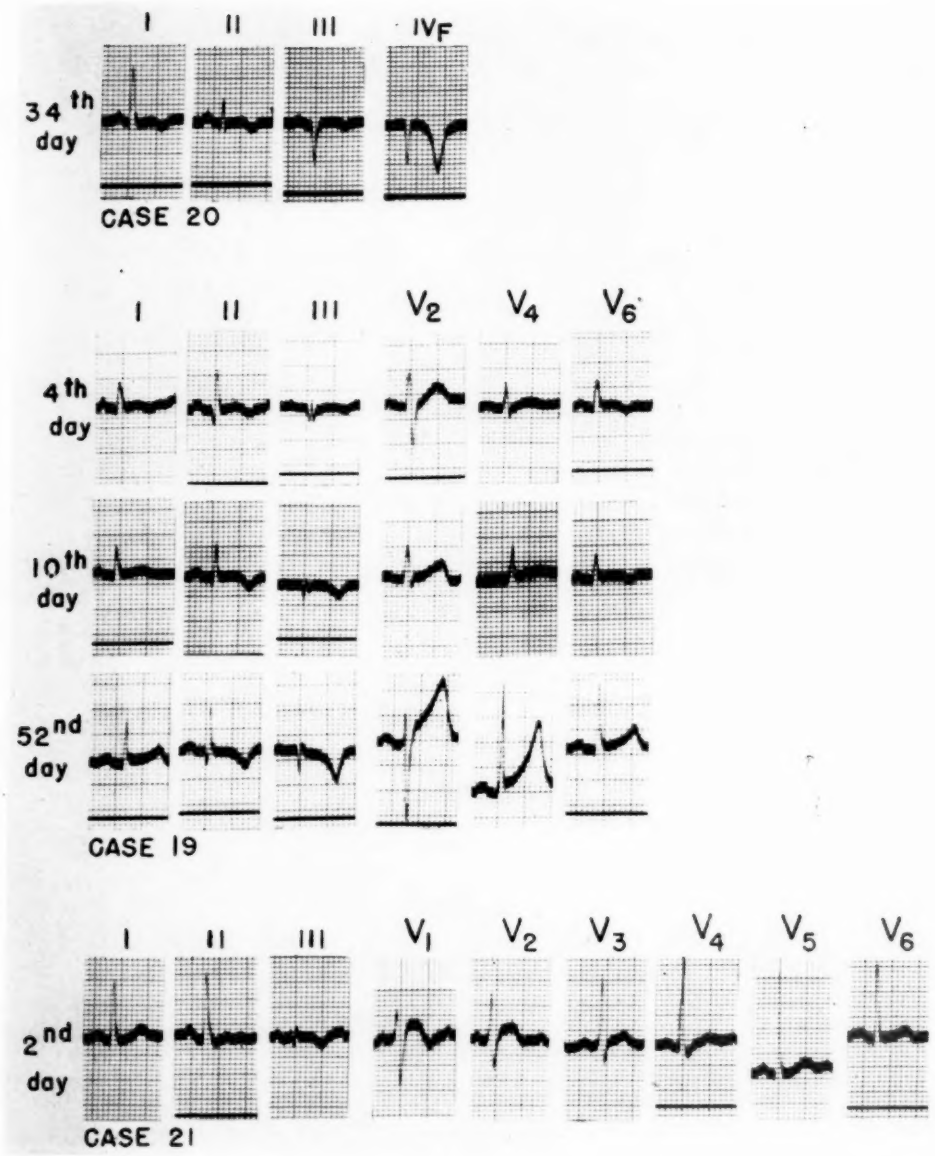

Fig. 7.—Electrocardiograms in cases without operation.

Case 20. Q wave and deeply inverted T wave in Lead IV F indicative either of a laceration of the descending branch of left coronary artery with resultant anterior myocardial infarction or a ventricular wound involving complete thickness of myocardium.

Case 19. Note (a) Q_2, Q_3 and T_2, T_3 pattern, tall T waves in precordial leads at fifty-two days, indicating localized damage to posterior basal aspect of left ventricle either as direct result of wound or through infarct caused by laceration of right coronary artery. (Patient was stabbed in the back with a long knife.)

Case 21. Isolated elevation of R-TV_{1+2} suggests subepicardial myocardial process localized over right venticle.

was obtained. This patient, a Negro 26 years of age, was stabbed in the back with a long knife in two places, both between the levels of the second and fifth dorsal vertebrae, with resulting left-sided hemopneumothorax. The initial period of shock was short, the degree of anemia only moderate, and the Kline test of the blood serum for syphilis negative. There were no symptoms or findings of cardiac failure. Cardiac examination revealed a pericardial rub on the second day and a roentgenogram showed slight cardiac enlargement. At first there was displacement of the mediastinum to the right, but this and the pleural effusion had practically disappeared by the eighteenth day. The well-marked Q and T patterns in Leads II and III may have been due merely to the wound of the posterior basal portion of the left ventricle, but in spite of the uneventful clinical course it is suspected that the right coronary artery was lacerated with the resulting electrocardiographic findings which are classical for an infarct in this area.

The other patient (Case 20), a Negro 27 years of age, presented an oblique laceration two inches long in the third left intercostal space near the midclavicular line, with resulting left hemopneumothorax. The postoperative course was stormy with tachycardia and dyspnea. The same considerations apply to the question of laceration of a coronary artery in this case as in the one just discussed.

A third case (Case 21—Fig. 7) shows elevation of the R-T segments in Leads V_1 and V_2 only, which is regarded as suggestive evidence of early subepicardial myocardial damage over the right ventricle. There are no localizing findings in the remaining two cases.

Follow-up Studies.—The purpose of this part of the study was threefold: first, to obtain electrocardiograms at a late enough date to avoid the complicating patterns of pericarditis; second, to attempt to correlate the electrocardiographic findings with other evidence bearing upon the cardiac status of these patients; and third, to look for evidences of constrictive pericarditis. The first aspect of this study has been incorporated into the preceding discussion, but these late electrocardiographic findings are listed in Table V for comparison with Tables II and III.

The symptoms and physical, roentgenologic, and electrocardiographic findings in eight patients examined by me at periods varying between five and thirty-six months following a cardiac wound are shown in Table VI. It is notable that in the first three cases with normal electrocardiograms all other objective findings are likewise entirely normal. However, all of these patients have symptoms. None of these are clearly of cardiac origin, and in each case there are unmistakable evidences of neurosis. The remaining five patients have abnormal electrocardiograms. In three of these other definite objective evidences of cardiac damage are present. In two the only other objective abnormality is the fluoroscopic finding of apical pleuropericardial adhesions not extensive enough to be clinically significant. Thus in the cases of these two patients the electrocardiographic findings are the only definite evidence of residual cardiac damage. In Case 1 the physical and roentgen findings are probably

TABLE VI. FINDINGS IN FOLLOW-UP STUDIES OF EIGHT PATIENTS

CASE	TIME OF FOLLOW-UP (MONTHS)	SYMPTOMS	CARDIAC FINDINGS	VENOUS PRESSURE (CM. H_2O)	ROENTGEN FINDINGS	ECG
13	11	Precordial heaviness; slight dyspnea; questionable orthopnea; numbness and "weakness" of left side of chest since blow to operative site sustained at factory	Normal size; no murmurs; B.P., 120/88; no pulsus paradoxus; no precordial retraction	6.7	Normal-sized heart on 7-foot plate taken at 3½ months	Normal
21	5	Nervousness; slight dyspnea; slight palpitation	Normal size and sounds; no murmurs; B.P., 124/88; no precordial retraction	—	Normal-sized heart on previous 7-foot film.	Normal
23	11	Nervousness; poor general health; precordial sticking pain, progressive dyspnea (patient's husband in prison; she requires welfare assistance)	Normal size and sounds; no murmurs; B.P., 108/78; no evidence of cardiac failure; no precordial retraction	9.0	Heart normal in size and contour on 7-foot film	Normal
1	35	None; returned to work two weeks after discharge from hospital; can easily run a block	Moderate enlargement; tambour aortic second sound; no murmurs; B.P., 194/116; no precordial retraction; grade 11+ hypertensive retinopathy	10.8	Moderate enlargement of hypertensive type; slight diffuse aortic dilatation; cardiac pulsations not forceful but no localized bulging during systole	Right ventricular myocardial damage; left ventricular hypertrophy

6	36	Has not worked since, "afraid to strain my heart"; questionable dyspnea; precordial aching	Apical impulse within midclavicular line; occasional premature systoles; no murmurs; normal sounds; B.P., 130/96; heart shifts with change of position; no pulsus paradoxus	7.0	Minimal lag in contraction at apex; slight left ventricular enlargement	Left ventricular damage; probable old anterior infarct
8	8	Slight palpitation; substernal tightness; good exercise tolerance	Normal size; wide splitting of first cardiac sounds; very soft apical systolic murmur; B.P., 124/90	5.0	Heart normal in size and contour on 7-foot film	Left ventricular myocardcardial damage; prolonged A-V conduction
10	28	None; slight palpitation noticed for one year has disappeared	Skin retracts with systole in small area near sternum; normal size and sounds; no murmurs or pulsus paradoxus; B.P., 128/80	7.0	Pulsations of good quality; visible apical adhesion; normal size and contour on 7-foot film	Left ventricular damage
14	21	Has limited his activities but no symptoms during ordinary activities	Normal size; no murmurs; aortic second sound slightly accentuated; cardiac sounds somewhat distant; systolic precordial retraction; no pulsus paradoxus or Broadbent's sign; B.P., 134/90	7.0	Normal size and contour; no bulging during systole; apical pericardial scar	Left ventricular damage

due chiefly to the associated hypertensive heart disease, whereas the electrocardiogram shows the effect of this complication and also of the right ventricular damage caused by the wound. While two of these five patients presented symptoms which were hard to evaluate, both exhibited abnormal objective findings in addition to the electrocardiogram. Evidences of chronic adhesive pericarditis sufficient to cause systolic retraction of ribs, fixation of the heart, or pulsus paradoxus were not observed, and the venous pressure in the antecubital vein was found to be normal in the seven patients tested.

COMMENT

REVIEW AND DISCUSSION OF THE ELECTROCARDIOGRAPHIC FINDINGS AT VARIOUS STAGES.—

Early Stage (Preoperative and First Twenty-four Hours).—The findings among the thirty-one cases depicted in the literature are described in detail in the foregoing and are summarized in Table I. The findings among eight cases in the present series are presented in the description of the RS-T segment patterns of pericarditis, in Table IV, and are illustrated in Figs. 1 and 5. Combining the two series, there were nine patients with preoperative tracings. Three showed definite evidence of an anterior myocardial infarct; one, right bundle branch block; one, definite pericarditis; two, suggestive pericarditis; and one, nonspecific changes; one was normal. The findings in these cases have the most direct bearing upon the question of the value of the electrocardiogram in the preoperative diagnosis of cardiac involvement in a thoracic wound. They indicate that definite evidences of cardiac involvement may be found in a sizeable proportion of such cases but that occasionally normal or nonspecific patterns may occur. From the standpoint of operative criteria, the physical and fluoroscopic evidences of cardiac tamponade are more directly applicable.

In the combined total of thirty-nine patients with one or more tracings taken preoperatively and/or during the first twenty-four hours, the electrocardiograms were diagnostic of the presence of myocardial infarction, bundle branch block, or pericarditis in twenty-one instances and suggestive of one of these conditions in an additional nine instances. However, in spite of the fact that it is at this stage that shock, anemia, and displacements of the heart are most prominent and are added to the direct effects of the wound, there were five instances in which the electrocardiogram was essentially normal. In eight patients, including some with suggestions of other lesions, nonspecific abnormalities were present. In several instances when the first electrocardiogram was taken preoperatively or within a few minutes or hours following operation, subsequent tracings during the first twenty-four hours showed the appearance of evidences of pericarditis or infarction. Since shock, anemia, and displacements of the heart may occur in wounds of the thorax not involving the heart and may cause nonspecific electrocardiographic abnormalities including inversions of the T waves, these early electrocardiograms should be considered as indicating cardiac involvement only when patterns of infarction, bundle branch block, or acute pericarditis are present.

The first two of these patterns also provide information as to the site of the cardiac wound.

Early Intermediate Stage (Second Day Through the First Three Weeks).—The description by Herve and Forero Sarabia of the series of events taking place during this period is given in the foregoing and adequately covers the characteristic RS-T and T wave patterns as seen in tracings depicted in the literature. The findings in the present series are very similar, and since they are predominantly those of pericarditis, they are described under that section. Reference to Table IV and to Figs. 1, 2, 4, and 7 will disclose the details as seen in individual cases in the present series. The general uniformity of the patterns is due to the practically universal presence of pericarditis which produces very characteristic changes at this stage. Thus, the patterns are usually similar regardless of the location of the wound. The exceptions are instances of right bundle branch block, as illustrated by Case 5 of Fig. 3, and also instances of laceration or ligation of a coronary artery with resultant myocardial infarction. However, during the first few days of the early intermediate period, the characteristic reciprocal depression of the RS-T segment in Lead III occurring with anterior infarction usually disappears due to the opposing effect of the pericarditis which tends to cause elevation in all leads. This same sequence of effects has been observed in experimental myocardial infarction[2] and in clinical instances of coronary heart disease with myocardial infarction complicated by pericarditis.[1] The second distinctive feature in the cases with complicating infarction is the presence of abnormal Q waves. They tend to remain for months or years and so may occur at any of the stages being considered. The rare occurrence of the Q_2-Q_3 pattern of the posterior infarction in a cardiac wound is shown in Case 19 of Fig. 7. Esophageal and unipolar leads from the extremities would have contributed valuable confirmatory evidence in this case. In anterior infarcts, the pathologic Q waves are best seen in the precordial leads. Case 15 (Fig. 5) is the only anatomically proved instance of myocardial infarction in the present series, although it is likely that Case 6 of Fig. 5, and Case 20 of Fig. 7 are additional instances of anterior infarction. The alternate explanation of these Q- or diminished R-wave patterns is that they are due to the effects of a wound which involves nearly all or the complete thickness of the ventricular wall in the region underlying the exploring electrode. As mentioned previously, if the wound itself caused the Q waves, they might be expected to appear more frequently, especially when multiple precordial leads are taken. In either event they represent a localizing effect of the wound. The absence of Q waves in the precordial leads in instances described in the literature in which ligation of the left coronary artery or its branches is known to have occurred is explained either by the infarct's not extending through the full thickness of the wall or being localized to an area not influencing the single precordial electrode employed. The idea that more adequate collateral circulation exists in hearts with previously normal coronary arteries and that therefore infarction may not occur has been proved to be false by the studies of Blumgart and co-workers.[73]

In the first part of the early intermediate period, inversions of the T waves cannot be ascribed to pericarditis since it is known that they almost always

appear later in uncomplicated instances of this condition. Neither can they be considered as a direct effect of the cardiac wound since there is no discoverable relation between the leads in which they occur and the location of the wound. They are best considered as evidences of nonspecific myocardial damage and are probably often due to shock and anemia which are most marked at this stage. Occurrence of very deep T waves, such as those seen in the eighteenth day in Case 8 of Fig. 6, suggest myocardial damage rather than pericarditis because the latter is less often responsible for inversions of this depth.

Late Intermediate Stage (Three Weeks Through Three Months).—The point of greatest interest concerning the late intermediate stage is whether or not the effects of pericarditis disappear sufficiently so that patterns due to the cardiac wound itself can be recognized. As previously mentioned, the opinion has been expressed[31,53] that this is possible after the second week. However, a review of the literature on the persistence of the effects of pericarditis of various other types does not support this opinion. Thus, Winternitz and Langendorf[58] stated that the T waves usually became inverted during the third week and that the inversion might last for several months, although this abnormality always disappeared later when healing had occurred. Holzmann,[71] in classifying the electrocardiographic changes during pericarditis, placed the "late acute phase" between the tenth day and the sixth week, the subacute stage between six weeks and two months. Perhaps the best idea of how long the electrocardiographic effects of the type of pericarditis accompanying cardiac wounds may persist is gained from a review of cases of atrial or pericardial wounds in which the persistent T-wave inversions are necessarily associated with the pericarditis, since these structures have no direct effect on the T waves. There are five cases[6,15,53] (CASES 25,26,30) suitable for this purpose depicted in the literature. T-wave abnormalities are still present at forty-three, fifty-two, sixty, sixty, and ninety days. In two similar cases in the present series, abnormalities are present in the last electrocardiograms at twenty-four and ninety-seven days (Fig. 1).

There is some additional evidence for the persistence of the effects of pericarditis during this period. In Case 12 of Fig. 2 the reversal from negative to positive of the T wave in Lead I and the reappearance of elevation of the RS-T segment in Lead IVF in the tracing taken on the thirty-first day are characteristic of an acute flare-up of pericarditis. This makes it hazardous to consider the next tracing in this same case taken only fourteen days later which conforms to the so-called "late T_1 pattern" of left ventricular wounds as definitely due to the localized effect of the wound rather than to subacute pericarditis. The close similarity between the tracing at twenty-six days in this case to that of twenty-four days in Case 2 of Fig. 2 and that of twenty-three days in Case 4 of Fig. 4, both of the latter two occurring in wounds of the right ventricle, further illustrates the difficulties of ascribing localizing significance to changes in the T waves during this period. Case 3 of Fig. 4 illustrates the so-called "late T_2-T_3 pattern" of right ventricular wounds. While it is true that many types of right ventricular myocardial damage are reflected in these leads, it is also true that uncomplicated pericarditis may cause inversions of the T waves in these leads

alone.[69] Since it has been shown that pericarditis is frequently still active, it is doubted that such a pattern should be considered at this time as definitely due to the direct effect of the right ventricular wound.

Late Stage (Three Months or More After the Wound).—Excluding patients with complicating myocardial infarction, the three standard leads in approximately 50 per cent of patients with persistently abnormal tracings (Tables II and V) correspond very well with the previously described "late T_1 pattern" of left ventricular wounds and in most instances with the "late T_2-T_3 pattern" of right ventricular wounds. In the former the T wave in Lead I was always abnormal, whereas combined abnormalities of the T waves in Leads II and III did not occur. In the right ventricular wounds only one case showed T-wave abnormalities limited to Lead I, whereas the remaining cases showed either the T_2-T_3 pattern or right bundle branch block. This correspondence with the previously described T-wave patterns which were based upon electrocardiograms taken at periods from two weeks onward suggests that these patterns may appear earlier than three months. However, they are not as reliable then as later.

Among the cases depicted in the literature with a single precordial lead, there was only one patient in whom it was entirely normal. In two patients it constituted the chief although not the only abnormality. Its T wave was inverted in both right and left ventricular wounds as might be expected from its location, which usually overlies the vicinity of the interventricular septum and so exposes it to influences from either ventricle. For this reason and also because from experience in other diseases of the heart it is known that a single precardial lead may not record some right ventricular or lateral left ventricular lesions, multiple precordial leads would be expected to be superior in detecting small lesions and in indicating the location of the wound. This appears to be so as judged by the findings in these leads in the present series of patients. All of the patients with left ventricular wounds with persistently abnormal tracings showed abnormal T waves in Lead V_6, and all but one had abnormal T waves in Lead V_5, but there were three patients in whom this deflection was normal in Lead V_4. Since the location of this lead is the same as that usually chosen for a single precordial lead, the evidences of myocardial damage in these patients would have been missed by such a lead. While there was only one patient with a right ventricular wound in whom the tracings were abnormal at this stage, the T wave in Lead V_6 was upright and the maximum inversion occurred in Lead V_4, which corresponded to the location of the wound in the right ventricle near the septum.

Until these late tracings were obtained, there seemed to be some question as to whether the wound itself, in the absence of damage to a coronary artery or to the branches of the bundle of His, caused any detectable electrocardiographic changes. However, the later emergence of these patterns indicates that they were present earlier but usually indistinguishable from the changes due to pericarditis.

Follow-up Studies in Cardiac Wounds.—Apart from the electrocardiographic findings, no attempt has been made to review the literature concerning the

late results of penetrating cardiac wounds. As mentioned previously, there have been only thirteen cases with published electrocardiograms followed for more than six months. The most extensive study of late electrocardiographic and other clinical findings is that of Steffens,[74] although in it the electrocardiograms are not published. His 109 patients were German veterans of World War I who had sustained bullet wounds from ten to twenty years before re-examination. In only ten of the sixty-nine cases studied electrocardiographically with the standard leads from the extremities were the tracings abnormal. In several of these patients there was complicating disease of the heart sufficient to account for the abnormalities. In the remaining patients there were no other objective evidences of myocardial damage. Of the whole group, however, only 13 per cent had no complaints. For the most part, the symptoms were considered as psychogenic.

In the present study also the electrocardiograms exhibited the most constant and persistent objective abnormality. Because of this they are of value in indicating the need for some caution in the management of such cases, although the patient's symptoms and physical and roentgen findings must also be considered. In patients who have indefinite symptoms of a type suggesting a psychoneurosis, but whose physical and roentgen examinations disclose no abnormalities, the finding of a normal electrocardiogram, particularly when multiple precordial leads are taken, is strong evidence in favor of the functional origin of the complaints. It indicates the prime necessity of psychotherapy in their management.

SUMMARY AND CONCLUSIONS

1. A review of the literature on the electrocardiogram in penetrating wounds of the heart is presented including a tabular summary of thirty-one cases in which tracings were obtained during the first twenty-four hours and of an equal number in which they were taken three months or more (average, 7.1 months) after the wound.

2. The electrocardiographic findings in twenty-three similar cases observed at Detroit Receiving Hospital are described and illustrative examples presented. In sixteen of these cases, multiple precordial leads were obtained and in twelve the follow-up period was three months or longer (average, 18.5 months). Eight patients were completely re-examined by me at periods varying between five and thirty-six months (average, 19.1 months) following the wound, thus making possible a correlation of the symptoms and physical and roentgenologic findings with the electrocardiograms at this late stage.

3. In the present series of twenty-three patients, definite electrocardiographic evidences of pericarditis appeared in seventeen, in seven of whom no other abnormalities could be detected. Definite localizing patterns directly attributable to the wound were present in ten. In five of these the localizing findings appeared in early electrocardiograms and consisted of right bundle branch block (one case) or Q-wave patterns due either to complicating myo-

cardial infarction from injury of a coronary artery or possibly in some instances to involvement of the full thickness of the ventricular wall by the wound itself. In the other five cases the localizing patterns were not well-defined until three months or more after the wound. Four of these were instances of left ventricular wounds characterized by abnormalities of the T waves in Lead I and in one or more of the precordial Leads V_4, V_5, and V_6. The one instance of a right ventricular wound in which a late tracing was obtained showed abnormalities of the T waves in Leads V_3, V_4, and V_5, corresponding closely with the location of the wound in the right ventricle near the septum.

4. The clinical follow-up studies on eight patients in the present series indicates that the electrocardiogram exhibits the most persistent objective abnormalities. When present, they suggest the need for some caution in the management of the patient. When the electrocardiogram is normal in all leads, including those taken from multiple precordial stations, it is of aid in confirming the psychogenic origin of persistent subjective symptoms.

As judged by the findings in the present series and in those in which the electrocardiograms are depicted in the literature, the following conclusions are drawn:

1. Preoperative electrocardiograms show definite evidences of cardiac involvement in the majority of cases and therefore may aid in the decision as to whether or not the heart is included in a thoracic wound. Electrocardiographic findings such as those of pericarditis, bundle branch block, or myocardial infarction may be accepted as definite evidences of cardiac involvement, whereas T-wave abnormalities and minor deviations of the RS-T segments cannot be relied upon since they could be caused by shock, anemia, or displacements of the heart which are often present in thoracic wounds without cardiac involvement.

2. During the first twenty-four hours the incidence of abnormal tracings increases. Changes due to pericarditis frequently appear but usually at this time do not obscure the RS-T segment and T-wave patterns of myocardial infarction due to laceration or ligation of a coronary artery.

3. During the early intermediate period (second day through the first three weeks) the effects of pericarditis predominate and cause strikingly similar findings in the majority of the cases regardless of the location of the wound. The RS-T segment and T-wave changes of anterior myocardial infarction likewise may be obscured, although a sufficient number of precordial leads would be expected to show Q waves in most of such cases.

4. During the late intermediate period (three weeks through three months) the electrocardiographic effects of pericarditis may persist. This makes the T-wave patterns unreliable at this time for locating the site of the wound. In this period and in all of the previous periods localizing findings are provided chiefly by either bundle branch block or indirectly by Q-wave patterns of infarction.

5. The consistent finding of abnormalities of the T waves limited to one or more of the precordial Leads V_4, V_5, and V_6 in late tracings of patients with left ventricular wounds amplifies the previously described "T_1 pattern" and demon-

strates the superiority of such leads over a single precordial lead. The late tracing of one patient with a wound of the right ventricle, as well as clinical experience with multiple precordial leads in other right ventricular lesions, suggests that such leads may be expected to yield information not afforded by a single precordial lead and should amplify the previously described "T_2 pattern."

6. The failure to find differences in the electrocardiographic patterns resulting from wounds of different parts of the heart or between those with and without interruption of a sizeable coronary artery is usually due to the obscuring effects of pericarditis in most tracings except those taken either very early or after several months have elapsed. It may also be due to an insufficient number of leads or to not recognizing the distinctions between patterns of pericarditis and myocardial infarction.

7. Further investigation is needed to clarify two interesting questions raised by the findings in multiple precordial leads in the present study: (A) May the wound itself produce Q waves in one or more of these leads, or are these always due to an area of myocardial infarction from interruption of a coronary artery? (B) Is the progressive disappearance of inversion of the T waves in some of the precordial leads entirely due to the recession of generalized pericarditis, or may it be due partly to a decrease in the size of the wound and thus give valuable evidence of the healing process?

The author wishes to express his thanks to Dr. Morris H. Blau and other members of the Surgical Department for their help and cooperation in this study. Also he wishes to thank Dr. Gordon B. Myers for helpful advice and criticism.

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ADDENDUM

Since this article was submitted for publication, four of the five patients with persistently abnormal electrocardiograms listed in Table VI (Cases 6, 8, 10, and 14) were re-examined during August through October, 1946, approximately two years following the examination recorded in Table VI.

Their status as far as the presence or absence of symptoms is concerned remains unchanged except for the occurrence of mild dyspnea upon exertion in Case 8. Physical examination revealed no notable change in cardiac findings and no pulsus paradoxicus or venous distention in any case. Moderate hypertension appeared in Case 10. Roentgenograms were practically identical in all cases except Case 10, in which there was an increase in the transverse diameter of the heart of 0.5 centimeter. The slightness of the change and the presence of some rotation of the thorax negated the significance of this finding. The electrocardiogram in Case 6 showed disappearance of low voltage, a change in the T waves in Lead I from isoelectric to diphasic, those in Lead V_4 from diphasic to inverted and persistence of T-wave inversion in Leads V_5 and V_6. These changes in the T waves might have been due to a change in the position of the heart from an intermediate to a semivertical position. In Case 8 prolonged auriculoventricular conduction persisted, but the T waves in Leads V_4 and V_5 were slightly less deeply inverted. The T waves in Lead V_2 became diphasic from normally upright. In Case 10 there was no significant change in the electrocardio-

gram. In Case 14 the T waves in Leads I, II, and V_6 became low upright from diphasic and those in Leads V_4 and V_5 normally upright from low upright and diphasic, respectively.

In summary, during this two-year period there was little change in the history, physical, or roentgenographic findings in these four patients. The electrocardiogram of one patient remained unchanged, those of two showed minor changes, while that of the fourth patient revealed definite improvement in the status of the myocardium.

A CLINICAL EVALUATION OF POWDERED HUMAN BLOOD CELLS IN THE TREATMENT OF ULCERS OF THE EXTREMITIES ASSOCIATED WITH VASCULAR DISORDERS

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THE treatment of ulceration of an extremity which is affected by vascular disease is frequently a serious problem. The ischemic ulcer associated with occlusive arterial disease is notoriously indolent and resistant to local or topical applications. It may have been produced by major or minor trauma or local infection or it may persist after the sloughing of gangrenous tissue. It may occur at the site of amputation of a digit or portion of a limb. It is usually infected and its base is frequently choked with leucocytes. Because of ischemia the tissue at the base and margin of the ulcer is very sensitive to heat, cold, and chemical irritation. Detergents or other topical applications which have even the slightest tendency to cytotoxicity may affect such ulcers adversely. The use of ointments or wet dressings is often tolerated poorly. The ulcers are frequently painful. In spite of measures designed to produce vasodilatation and improve arterial blood flow, they may persist for weeks or months and cause prolonged suffering and disability.

The so-called stasis ulcer associated with chronic venous insufficiency which follows thrombophlebitis or complicates extensive primary varicose veins is somewhat less serious and may be easier to heal. However, it is often large, indolent, and infected, particularly when neglected. Many such ulcers will respond favorably to rest in bed with elevation of the limb and the application of almost any bland wet dressing. Stasis ulcers, also, are sensitive to strong or irritating solutions, ointments, or powders. Some are very resistant to any type of treatment and even take skin grafts poorly.

The use of concentrated human blood cells both in the form of the natural gelatinous mass and in the form of dried powder as a topical application arose from the attempt to utilize this by-product of plasma extraction. There is considerable evidence that healing processes are promoted by blood cells. Nature provides a crust of clotted blood over lacerations and abrasions of the skin. Under this crust granulation and epithelization progress. The crust undoubtedly serves as a protection from exogenous contamination and may be a nutritive supply for the reparative process. Dentists dread the occurrence of "dry sockets" following extractions, in which there is no clot to organize, contract,

Received for publication April 29, 1946.
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and fill the defect. Seldon, Lundy, and Essex[1] actually observed accelerated growth of vascular and connective tissue in the rabbit ear in the presence of an old hemorrhage.

Naide[2] reported promising results in eleven of fifteen cases in which he removed blood from the patient's antecubital vein and allowed it to clot in an ulcer crater. Moorhead and Unger[3] first used as a dressing for ulcers the gelatinous mass of concentrated human blood cells from which the plasma had been extracted. They were impressed by the decrease of purulent secretion, stimulation of healthy granulations, and the impervious covering which was created.

Difficulty was experienced in the handling of human blood cells in their wet form in their early use at the Mayo Clinic. For that reason one of us (T. H. S.) proposed the use of dried and powdered human blood cells. In an earlier report, Seldon and Young[4] outlined the method of preparation and technique of application. As a result of these and subsequent observations, it was felt that the favorable effects of dried and powdered blood cells in the healing of wounds and ulcers were due to some nutritive factor within the cells which is more or less specific in its action.[4-6]

Murray and Shaar[7] prepared a paste of red cells with tragacanth and hexylresorcinol. They observed more constant relief of pain with this mixture than with the powdered form. In addition to the nutritive and protective property hypothesized by other observers, they expressed the idea that the crust also serves as a mechanical scaffolding to support epithelization.

It is our purpose in this publication to attempt an evaluation of the efficacy of powdered human blood cells in the treatment of chronic ulcers of patients admitted to the hospital service for peripheral vascular diseases. All of the patients had definite vascular insufficiency as the basis for the ulcerations. The patients were entirely unselected in that they included all those treated with blood cells over a period when they came under the observation of one or all of us.

Needless to say, a controlled study comparing the results of various forms of local treatment for vascular ulcers of human beings is an impossibility since no two patients present lesions of identical size, duration, and character with identical underlying vascular pathologic changes. Conclusions must, therefore, be based largely on the clinical impression of the physician who has seen and treated similar patients. In many cases it was possible to compare the effect of powdered blood cells with that of other topical applications which had been used previously during the period of hospital treatment for the same patient.

MATERIAL AND METHOD

The series to be presented here includes forty-six patients divided primarily into two groups on the basis of the underlying vascular disease. In twenty-nine patients arterial insufficiency was the primary vascular factor, and in the remaining seventeen, venous insufficiency was the primary factor. A further breakdown of the cases into specific vascular diseases gives the following distribution: thromboangiitis obliterans, sixteen; arteriosclerosis obliterans, thirteen; post-thrombophlebitic venous insufficiency, ten; varicose veins with venous

TABLE I. THROMBOANGIITIS OBLITERANS

CASE	AGE (YR.) AND SEX	DURATION VASCULAR DISEASE (YR.)	DURATION ULCER (MO.)	SIZE OF ULCER (CM.)	LOCATION OF ULCER	DESCRIPTION OF ULCER	PREVIOUS TREATMENT	DURATION POWDERED BLOOD CELL TREATMENT (DAYS)	COMMENT
1	44 M	8	24	1 by 0.8 1 by 0.8	Dorsum R2 and 3 toes	Infected and ischemic	Various ointments, boric acid dressings	15	Good result; 75 per cent healed
2	55 M	17	4	1 by 0.5 1 by 1	R2 toe	Gangrenous and deep	Boric acid soaks, sulfathiazole ointment, tyrothricin dressings	34	Fair result; healed to bone exposed in base; osteomyelitis of phalanx
3	38 M	4	2	1.5 by 1	Subungual R1 toe	Crusted and oozing	Boric acid soaks, nail removed, tyrothricin dressings	9	Fair result; practically healed
4	36 M	2	2	1 by 1	Plantar L1 toe	Indolent and gangrenous	"Callus cure," sulfathiazole ointment, tyrothricin dressings	23	Continued necrosis; guillotine amputation of L1 toe; 0.5 by 0.5 cm. residual ulcer healed in seven days with blood cells
5	52 M	10	3	Small	Web between L4 and 5 toes	Fissure, pale and ischemic	Fungicide, various ointments, potassium permanganate soaks	18	Good result; ulcer healed
6	55 M	4	3	2 by 3	Dorsum L foot	Deep and gangrenous	Boric acid and tyrothricin dressings	27	Fair result; ulcer healed; blood cells used alternately with boric acid soaks
7	25 M	3	9	2 by 2	L5 toe	Gangrenous	Chemical cautery, sulfathiazole ointment, débridement	11	Good result; practically healed

8	35 M	2	1	2 by 2	R1 toe	Deep and necrotic	Various ointments, roentgen therapy, boric acid and tyrothricin dressings	20	Good result; healed
9	47 M	9	108	2.5 by 2	R1 toe	Irregular gray exudate	Fungicide, various ointments, boric acid and potassium permanganate soaks	23	Good result; healed
10	43 M	5	4	Small (3)	R5 toe R4 toe R3 and 4 toes	Infected and superficial	Fungicides, boric acid and potassium permanganate soaks	30	Good result; healed
11	45 M	10	8	5 by 3	R1 toe and foot	Purulent and ischemic	Removal of metatarsal bone, guillotine amputation R1 toe, tyrothricin dressings	28	Good result; almost healed
12	49 M	4	24	1.5 by 1.5	R1 toenail bed	Deep and necrotic	Curettage, tyrothricin dressings	19	Good result; ulcer healed
13	38 M	8	4	3.8 by 2.5	L ankle	Indolent, stasis	Boric acid dressing	10	Good result; ulcer healed
14	29 M	4	2	1 by 1	R1 toe	Infected and ischemic	Boric acid and tyrothricin dressings; sequestrum removed	19	Good result; ulcer healed
15	33 M	1½	6	3.5 by 2.5	L foot and L5 toe	Gangrenous; osteomyelitis of 5 metatarsal	Sulfathiazole ointment, boric acid soaks	58	Fair result; ulcer healed
16	29 M	8	1½	3 by 3	R1 toe amputation site	Gangrenous	Boric acid and tyrothricin dressings	35	Fair result; 80 per cent healed; rapid progress on dismissal

TABLE II. ARTERIOSCLEROSIS OBLITERANS

CASE	AGE (YR.) AND SEX	DURATION VASCULAR DISEASE (YR.)	DURATION ULCER (MO.)	SIZE OF ULCER (CM.)	LOCATION OF ULCER	DESCRIPTION OF ULCER	PREVIOUS TREATMENT	DURATION BLOOD CELL THERAPY (DAYS)	COMMENT
17	63 M	3	1	2 by 2 2 by 2	Dorsum L foot L1 toe	Infected and ischemic	Boric acid and tyrothricin dressing, sulfathiazole ointment	20	Fair result; apparently healed; polycythemia vera
18	60 M	5	3	3 by 3	Amputation site of L4 and 5 toes	Purulent and infected	Amputation of toes, boric acid dressings	17	Fair result; ulcer healed to exposed bone; osteomyelitis of 4 metatarsal; polycythemia vera
19	58 M	1	1	0.5 by 0.5 0.2 by 0.2	R2 and 5 toes	Ischemic and dirty	Various ointments, boric acid soaks	15	Fair result; ulcer 2 toe healed; ulcer 5 toe improved; diabetes mellitus; polycythemia vera
20	55 M	5	24	Multiple small and large	R and L lower legs	Circumscribed, deep, infected	Tyrothricin dressings	30	Fair result; all ulcers healed; polycythemia vera with stasis
21	35 M	2	¼	1 by 1	Bursa L1 toe	Necrotic	None	9	Fair result; tiny persistent opening into bursa
		3	2	1 by 1	L ankle	Crusted and necrotic	Boric acid dressings	14	Fair result; definite healing
		4	2	2.5 by 2 1.2 by 1	L foot and shin	Deep and necrotic	Boric acid and penicillin dressings	30	Fair result; two small ulcers healed; large ulcer 30 per cent healed

22	63 M	15	5	6 by 3.5	R knee	Gangrenous, foul slough	Sequestrectomy, various ointments, boric acid and tyrothricin dressings	108	Good result; ulcer healed; severe ischemia
23	57 M	8	10	3.8 by 3	L shin	Indolent, deep, infected	Various ointments, boric acid and tyrothricin dressings	9	Good result; 66 per cent healed
24	71 M	2	3	1 by 1	L1 toe	Osteomyelitis L1 toe, infected	Nail removed, boric acid dressings	5	Good results; healed except for pinhole sinus
25	44 M	2	2	1 by 1	L1 toe	Gangrenous	Chiropody, boric acid soaks, sulfathiazole ointment	8	Fair result; improved
26	54 M	1	12	5 by 10	L ankle	Deep, painful, infected	Various ointments, boric acid dressings	40	Good result; practically healed
27	64 F	¼	3	1 by 1.5 1 by 1	L and R ankles	Blue and painful	Various ointments, tyrothricin dressings	7	Fair result; 80 per cent healed
28	47 M	1/6	2	3 by 3 by 2	R foot, plantar	Deep and necrotic	Boric acid dressings	25	Good result; ulcer healed; diabetes mellitus
29	61 M	15	1	1.5 by 1.5	R1 metatarsal	Large, deep necrotic	Boric acid and tyrothricin dressings, sulfathiazole ointment	89	Poor result; some improvement; base of ulcer on joint capsule; diabetes mellitus

TABLE III. VENOUS INSUFFICIENCY—RESIDUAL OF PREVIOUS THROMBOPHLEBITIS

CASE	AGE (YR.) AND SEX	DURATION VASCULAR DISEASE (YR.)	DURATION ULCER (MO.)	SIZE OF ULCER (CM.)	LOCATION OF ULCER	DESCRIPTION OF ULCER	PREVIOUS TREATMENT	DURATION BLOOD CELL THERAPY (DAYS)	COMMENT
30	52 F	15	4	5 by 3	L medial malleolus	Infected and irregular	Various ointments, boric acid dressings	10	Good result; ulcer healed
31	42 M	14	3	Large	R shin	Infected and irregular	Long saphenous ligation, boric acid dressings	4	Good result; slow healing with boric acid; accelerated with blood cells
32	42 F	14	12	5 by 2.5	R medial malleolus	Indolent, infected	Attempted skin graft, long saphenous ligation	24	Good result; ulcer healed
33	46 F	23	23	2 by 2 2 by 1	L and R ankles	Indolent	Various ointments, long saphenous ligation	13	Good result; ulcers healed
34	70 F	2	2	11 by 16	R ankle	Indolent, superficial	Attempted skin graft, boric acid dressings	8 5	Poor result; generalized eczema developed

35	48 F	17	8	3 by 3	L ankle	Ragged, purulent plug	Boric acid and tyrothricin dressings	4	Fair result: apparently healed; ulcer was healing slowly with blood dressings
36	37 F	21	7	2 by 2	L ankle	Infected and irregular	Long saphenous ligation, boric acid and tyrothricin dressings	11	Good result; ulcer healed
37	38 M	16	5	3 by 2	L ankle	Indolent, gray slough	Boric acid and tyrothricin dressings	19	Good result; ulcer healed
38	42 M	28	5	15 by 10	L ankle	Painful, deep and foul	Various ointments, tyrothricin dressing	10 14	Fair result; ulcer granulating well; graft applied; marginal ulcers responded to blood cells
39	55 F	3	½	3 by 3	R calf	Chronic and infected	Boric acid dressings, various ointments	30	Fair result; 90 per cent healed

TABLE IV. PRIMARY VARICOSE VEINS WITH VENOUS INSUFFICIENCY

CASE	AGE (YR.) AND SEX	DURATION VASCULAR DISEASE (YR.)	DURATION ULCER (MO.)	SIZE OF ULCER (CM.)	LOCATION OF ULCER	DESCRIPTION OF ULCER	PREVIOUS TREATMENT	DURATION BLOOD CELL THERAPY (DAYS)	COMMENT
40	31 F	14	3	10 by 10	R ankle	Superficial and irregular	Boric acid dressings	6	Good result; ulcer healed
41	52 M	25	3	2 by 2 by 1	L ankle	Irregular and infected	Various ointments, boric acid and tyrothricin dressings	9	Fair result; ulcer improved—completed in ten days with boric acid and tyrothricin dressings
42	46 F	25	25	6.2 by 3.8	L ankle	Ragged, foul discharge	Long saphenous ligation, various ointments	28	Good result; ulcer healed
43	56 M	33	33	3 by 3 0.5 by 0.5	R and L ankles	Deep and jagged	Attempted skin graft, paste boots, various ointments	30	Fair result; small remaining ulcer healed after saphenous ligation
44	30 M	8	8	4 "large" ulcers	R and L ankles	Punched out, infected	Bilateral long saphenous ligation, boric acid dressings	6	Fair result; good granulation; graft applied
45	59 F	30	25	Large (6 by 8) 2 by 4	R shin L ankle	Irregular and deep	Long saphenous ligation, boric acid and tyrothricin dressings	27-L 23-R	Good result; almost complete healing
46	37 M	13	13	2 by 5	R ankle	Infected and dirty	Various ointments, boric acid dressings	6	Fair result; 50 per cent healed

insufficiency, seven. Diabetes mellitus complicated three and polycythemia vera four of the cases of arteriosclerosis obliterans.

Cultures were obtained from only fifteen ulcers. *Streptococcus hemolyticus* and *Staphylococcus aureus* grew in three cases (Cases 9, 10, and 44); *Staph. aureus* alone from six ulcers (Cases 15, 21, 27, 28, 37, and 45); *Str. hemolyticus* alone in one (Case 11); and *Escherichia coli* alone in one (Case 26). The other four cultures contained, respectively, diphtheroids, micrococcus, pseudomonas, and combined *Staph. aureus* and *Streptococcus viridans* (Cases 14, 20, 21, and 34).

On admission to the hospital, nearly all of the patients exhibited a certain degree of local cellulitis, active exudation, or gangrenous slough in or about the ulcer. Initial therapy to clean up the ulcer and surrounding tissue consisted usually of either soaks or dressings of warm saturated solution of boric acid or 0.5 per cent tyrothricin dressings. In a few cases potassium permanganate soaks (1:10,000 dilution), irrigation with penicillin solution, or application of 5 per cent sulfathiazole ointment was used for this same purpose. Many patients not included in this series showed good response to these measures, which were then continued, and local application of powdered blood cells was not used. For this reason, the ulcers which were treated with powdered blood cells were those which proved resistant to the usually accepted hospital regimen.

All patients received treatment which was aimed to relieve the underlying vascular disease. Those patients who had occlusive arterial disease were treated with rest in bed, warm environmental temperatures, and the Sanders oscillating bed. The use of tobacco was forbidden. Typhoid vaccine and lumbar sympathectomy were auxiliary vasodilating procedures employed in several cases of thromboangiitis obliterans. Phlebotomy and phenylhydrazine therapy supplemented local treatment in patients with complicating polycythemia vera. Diabetes mellitus when present was treated with diet and insulin. When venous insufficiency was the underlying factor, the involved extremities were kept elevated. Orally administered sulfadiazine or parenterally administered penicillin was used to treat spreading local infection whenever indicated.

Minor surgical procedures, such as removal of sequestra in underlying osteomyelitis and removal of nails in subungual lesions, were performed to give better exposure of the ulcers for local therapy (Cases 3, 4, 7, and 24). Two of the ulcers in patients with thromboangiitis obliterans were at the site of guillotine amputation for gangrenous toes (Cases 11 and 16). Blood cells were applied as adjuncts before and after skin grafting in two patients (Cases 38 and 44).

The mode of application and the method for preparing the powdered human blood cells were similar to those outlined in earlier reports from the Mayo Clinic.[5] After the ulcer had been cleaned with wet dressings, the powdered blood cells were applied with a sterile spatula or swab or dusted on from a container with a shaker top. The entire surface of the ulcer was covered with the powder and then loosely covered with a dry sterile dressing. Exudate absorbed from the tissues caused the powder to form a hard crust resembling that seen commonly on traumatic abrasions. Sometimes seepage from the ulcer caused the cell

crust to stick to the dressing and this was gently removed once daily. Any remaining serum was gently sponged from the bed of the ulcer with sterile sponges and a new layer of blood cells was applied. Eventually, as healing progressed, a point would be reached where the crust no longer stuck to the dressing. Then it was allowed to remain intact unless there was evidence of exudate underneath, which prevented contact between the cells and the bed of the ulcer. In these cases, the crust was loosened by soaking in boric acid solution or by applying dressings moistened with boric acid solution and was removed with a sterile forceps, and more powdered blood cells were applied. When healing was complete, the crust was either allowed to fall off spontaneously or was soaked until it softened enough to be peeled off.

RESULTS

Data concerning the cases in which powdered blood cells were used and results of this treatment are given in Tables I, II, III, and IV. In the final column is listed the condition of the ulcer at the time the patient was dismissed from the hospital or at the time powdered blood cell therapy was discontinued.

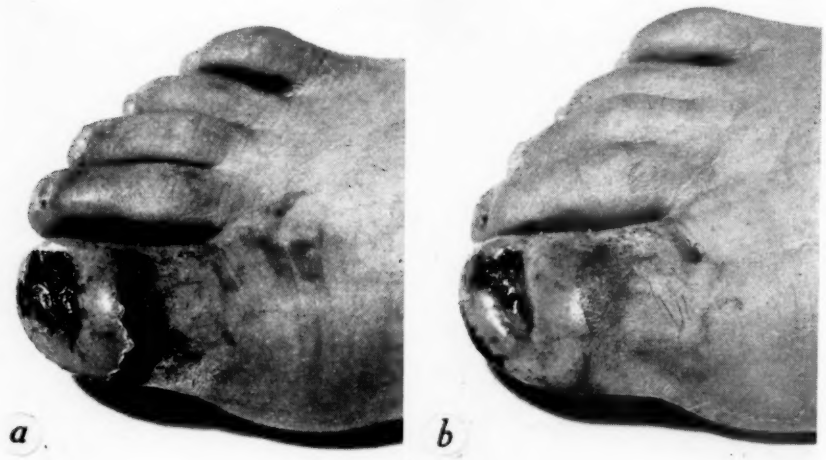

Fig. 1 (Case 12).—*a*, Thromboangiitis obliterans with gangrenous ulcer of bed of right first toenail. The ulcer had been present for two years. No evidence of healing was noted during local treatment with tyrothricin, after intravenous administration of typhoid vaccine, or after lumbar sympathetic ganglionectomy. *b*, Same ulcer almost healed seven days after treatment with powdered blood cells was begun. The ulcer was completely healed on the nineteenth day of treatment.

The results in those patients who left the hospital before complete healing occurred and who were given cells and instructions in their use at home are listed as percentage of ulcer healed (Cases 1, 11, 16, 21, 23, 27, and 46). Complete healing was prevented in some cases by the presence of exposed bone or a persistent sinus tract in the base of the ulcer (Cases 2, 18, 21, and 24). In two cases, powdered blood cells were used preoperatively and postoperatively where large defects were covered with split-thickness skin grafts (Cases 38 and 44). Treatment

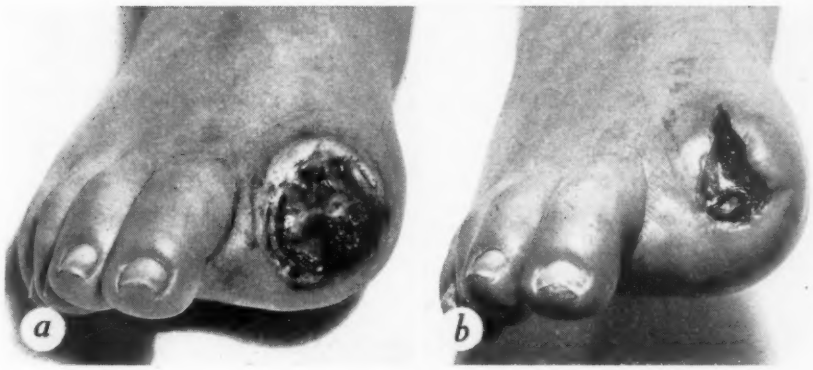

Fig. 2 (Case 16).—*a*, Thromboangiitis obliterans with ulcer at site of amputation of right first toe for gangrene. The patient had previously undergone lumbar sympathetic ganglionectomy. The ulcer was very painful and had failed to show any evidence of healing when treated with warm boric acid soaks, boric acid dressings, and tyrothricin during a period of six weeks. *b*, Same ulcer after treatment with powdered blood cells for thirty-five days. Pain was relieved and ulcer was 80 per cent healed.

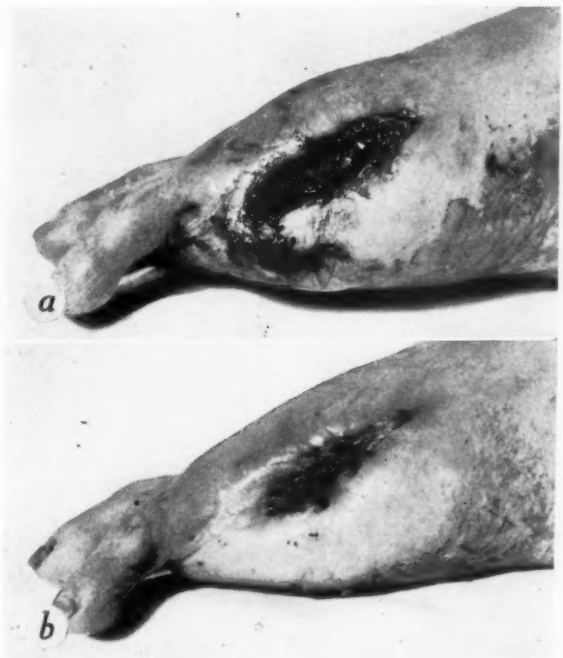

Fig. 3 (Case 11).—*a*, Thromboangiitis obliterans with deep gangrenous ulcer at site of amputation of right first toe and removal of distal half of right first metatarsal. The ulcer had been present for eight months. Tyrothricin wet dressings had been ineffective. *b*, Same ulcer almost completely healed after treatment with powdered blood cells for twenty-eight days.

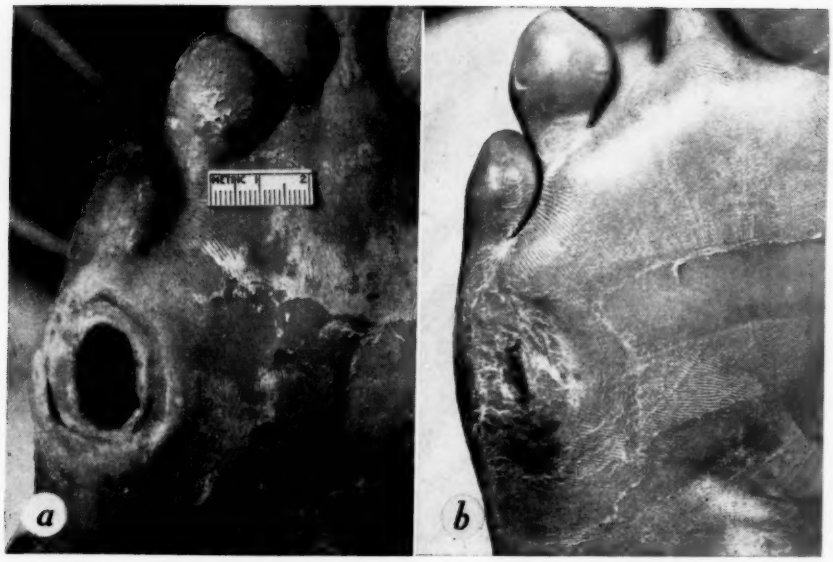

Fig. 4 (Case 28).—*a*, Arteriosclerosis obliterans with diabetes mellitus and infected ulcer in large callus over plantar surface of fifth metatarsal head. The ulcer had been present for two months. *b*, Same ulcer completely healed thirty-one days after treatment with powdered blood cells had been begun.

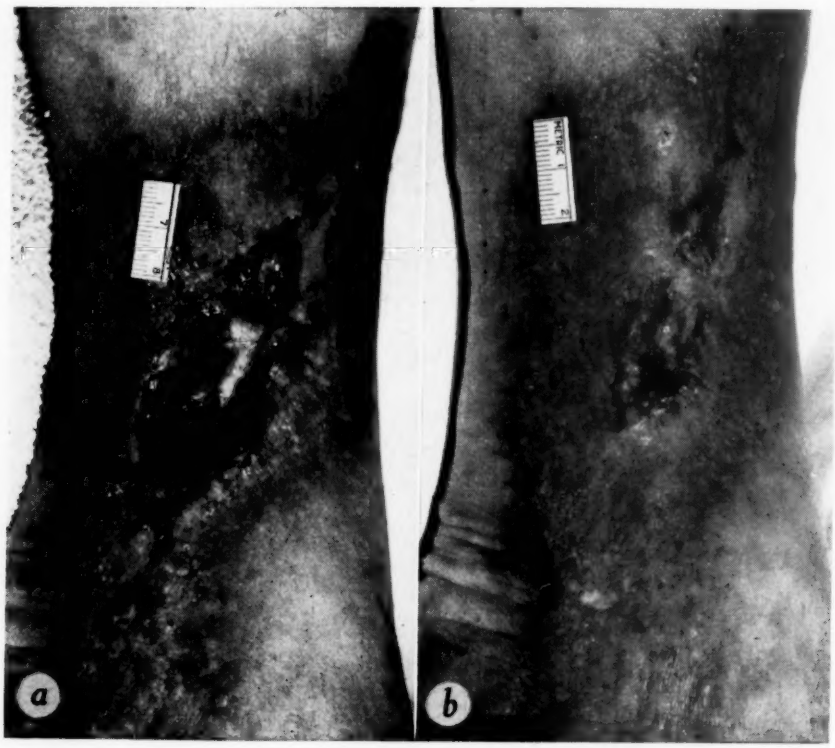

Fig. 5 (Case 42).—*a*, Primary varicose vein with chronic venous insufficiency and ulcer which had been present for more than two years. No healing had followed ligation and sclerosis of long saphenous vein and tributary varices. *b*, Same ulcer healed twenty-seven days after treatment with powdered blood cells had been started.

with powdered blood cells was discontinued in one case of stasis ulceration because of poor results (Case 34). In this patient severe generalized dermatitis developed. Powdered blood cells failed to control gangrenous ulceration in one patient with thromboangiitis obliterans in which guillotine amputation of a toe was required. Subsequently, the site of amputation healed rapidly during treatment with powdered blood cells (Case 4). Figs. 1 to 6, inclusive, show the results of treatment.

On the basis of observation on the progress of healing, Table V summarizes the results in the various types of vascular disease. In this table, good results

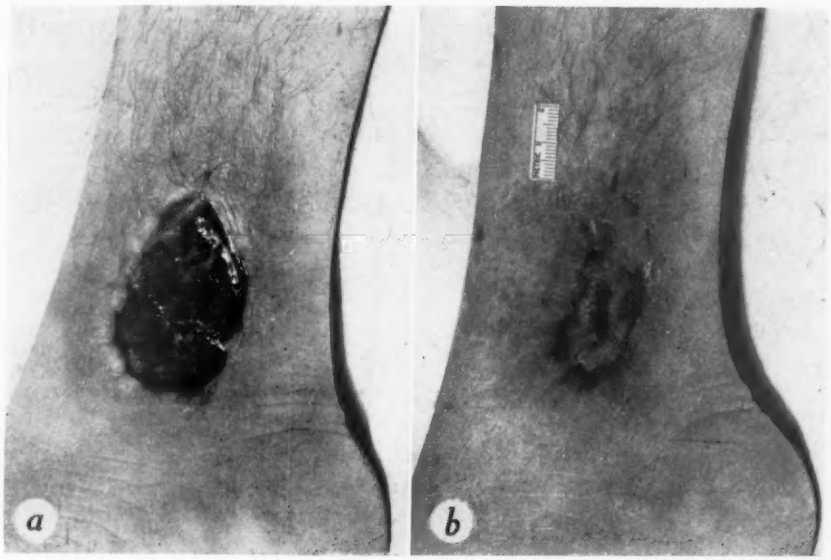

Fig. 6 (Case 32). —*a*, Chronic venous insufficiency caused by ancient iliofemoral thrombophlebitis with large ulcer of one year's duration at site of two previous ulcers. Attempted skin graft had failed one month before this picture was taken. *b*, Same ulcer healed twenty-four days after treatment with powdered blood cells had been started.

TABLE V. RESULTS OF TREATMENT WITH POWDERED BLOOD CELLS

DISEASE	CASES	RESULTS		
		GOOD	FAIR	POOR
Thromboangiitis obliterans	16	10	5	1
Arteriosclerosis obliterans	13	5	7	1
Post-thrombophlebitic venous insufficiency	10	6	3	1
Varicose veins with venous insufficiency	7	3	4	0
Totals	46	24	19	3

indicate that the powdered blood cells appeared to be superior to other local applications. Fair results indicate that the ulcers healed but probably not more rapidly than might have been expected with other local applications. Poor results indicate failure to heal or intolerance to treatment with powdered blood cells.

COMMENT

The use of powdered human blood cells as a topical application for chronic ulcers of the extremities associated with vascular disease is one of several methods of bland and nonirritating local treatment available to the physician. In order to evaluate its effect, we have reviewed a series of cases in which the patients were treated by this method at the Mayo Clinic. Despite the fact that patients with ulcers associated with venous insufficiency are more frequently seen on the hospital service than are those with ulcers associated with other types of vascular disease, fewer of these received this form of treatment since they frequently responded well to other bland local applications.

It is our impression that in approximately one-half of the patients with both the ischemic ulcers and stasis ulcers treated with the powdered blood cells, healing was much accelerated. This is based on previous experience with similar ulcers in patients with comparable degrees of vascular disease in whom other methods of local treatment were used and in those in whom a prolonged trial of other local applications had been made without evidence of healing before the powdered blood cells were used. In approximately one-half of the patients in whom powdered blood cells were used, it is questionable whether healing occurred any more rapidly than it would have with other bland local applications. In a few patients less healing occurred or the treatment was not well tolerated. Occasionally, it was necessary to alternate for periods of a few day's treatment with powdered red blood cells and treatment with bland wet dressings or tyrothricin solution.

It is difficult to determine whether the favorable response occurs from partial desiccation, from some healing factor in the cells, from nutrition supplied by the crust, or merely because the crust is protective and entirely nonirritating. Nevertheless, it is encouraging to observe progress in the ulcers, with first a puckering of the surrounding skin, then a freshening and reddening of the gray, avascular base, and finally granulations with epithelium creeping in from the margins. Certain disadvantages of wet dressings, such as maceration of the skin and chilling, are avoided with this "dry" method of treatment.

Care is necessary in removing the crusts and in applying the new dressing each day but, once the dressing has been applied, it need not be touched for twenty-four hours or sometimes longer. This has the advantage of simplicity and requires little time. Painful ulcers may become a little more painful during the first day the powdered blood cells are applied. After that, pain is usually relieved. Naturally, the use of blood cells in dealing with vascular ulcers is supplementary to the use of treatment to improve circulation and not a substitute for it.

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STUDIES ON THE VASCULARIZATION OF THE AORTA

I. The Vascularization of the Aorta in the Normal Dog

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THE possibility exists that diseases of the aorta are related to disturbances of the vascularization of its wall. This possibility was subjected to an experimental investigation in which (1) the vascularity of the aorta in several species of animals and in man in health and disease was studied by injection with radiopaque material and (2) the effects of experimental interference with this vascularization were analyzed.

In the present report the technique of studying the vascularity of the aorta is presented and the vascularization of the aorta in the normal dog is described.

TECHNIQUE

The hearts and aortas of fifty-seven dogs were obtained post mortem. The aortic vasa vasorum were injected in one of two ways. In the first method a glass cannula was inserted into the aorta, either at the arch or in the descending portion, facing upstream and tied firmly in place. All the branches of the aorta above the cannula except the coronary arteries were tied with catgut near their origin from the aorta. In the second method, one or two of the coronary artery branches, either of the right, of the left, or of both, were cannulated with the cannula facing upstream. Before injecting the coronary branch or branches, the coronary ostia in the sinus of Valsalva and the ascending aorta were occluded by means of wet cotton to prevent leakage into the aorta.

The injection material used was the gelatine-lead carbonate-mercuric sulfide mixture described by Dock.[1] It was injected under a pressure of between 150 to 200 mm. Hg in the various experiments by means of the apparatus developed by Schlesinger.[2] The aortas were opened and x-rayed; after the tissue was properly fixed, microscopic sections were prepared.† The x-ray technique used was: 40 kv.; 30 Ma.; 1½ sec.; a fine focal spot; anode-film distance, 30 inches; paper film holder and nonscreen film.‡

RESULTS

Ascending Aorta.—This study revealed that the ascending aorta of the normal dog is supplied (1) by vessels arising from the left and right coronary

From the Cardiovascular Department, Michael Reese Hospital.
Aided by the A. D. Nast Fund for Cardiovascular Research. This department is supported in part by the Michael Reese Research Foundation.
Received for publication May 4, 1946.
*Fellow of the Dazian Foundation.
†We are indebted to Dr. O. Saphir for the cooperation of the Pathology Department in preparing the microscopic sections.
‡We are indebted to Dr. R. Arens for the cooperation of the x-ray Department in obtaining the x-ray pictures.

arteries, (2) by vessels arising from the great vessels originating in the aortic arch, namely, the subclavian, carotid, and innominate arteries, and (3) by vasa arising directly from the lumen of the aorta. The vasa from these three sources form a rich anastomotic network (Fig. 1,). Since the dye used is too coarse to fill vessels less than 10μ in diameter, the anastomoses observed consist of vessels

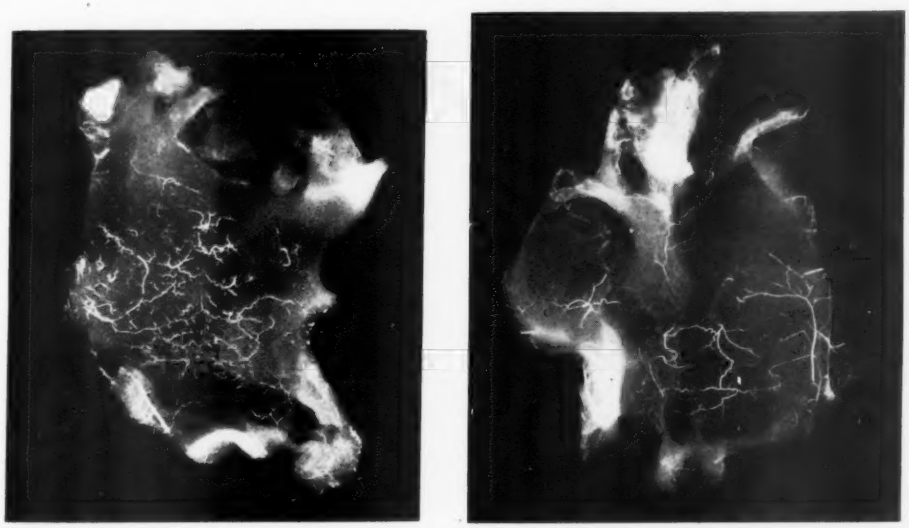

Fig. 1.—Injection of the vasa of the ascending aorta demonstrating their origin from both coronary arteries (below), from the vessels of the arch (above), and directly from the lumen of the aorta. Injection with cannula in the arch of aorta.

Fig. 2.—Injection of the first branches of the coronary arteries which supply the vasa of the ascending aorta.

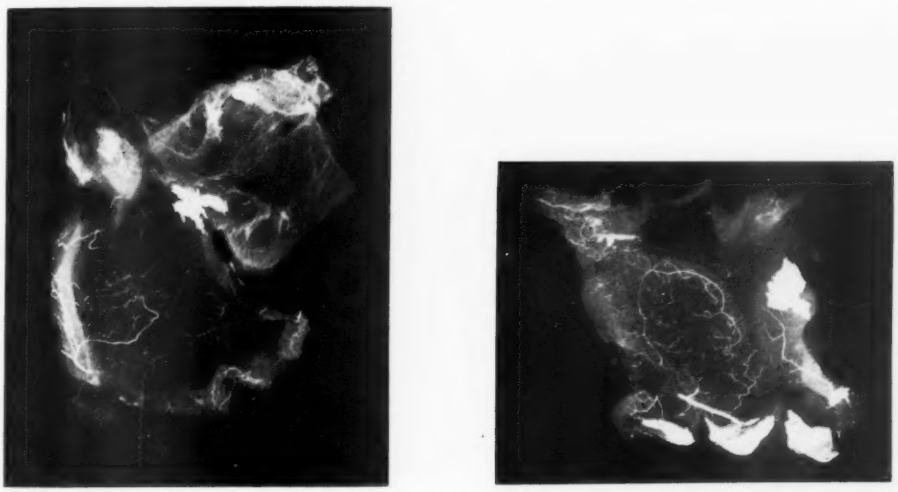

Fig. 3.—Anastomoses between the vasa arising from the right coronary artery and those arising from the left coronary artery. The left coronary artery was occluded at its orifice and the right coronary artery was injected by cannulation.

Fig. 4.—A preparation with an accessory ostium of the right coronary artery (the thick oblique vessel in the lower part of aorta). Note the predominance in the ascending aorta of the vasa arising from this coronary artery.

having three coats. The entire description of the vasa given below will therefore be confined to vessels of 10μ or more in diameter. Analysis soon revealed that the network was made up of (1) an adventitial network and (2) a medial network. The former was found to be far more extensive than the latter.

Adventitial Network: This network is supplied by vessels from the coronary arteries and from the large arteries of the aortic arch.

The first branches of the coronary arteries are the vasa to the aorta and pulmonary artery. These spread upward in the adventitia anteriorly and posteriorly over the ascending aorta. There are rich anastomoses between the branches of the left and right coronary arteries; anteriorly they are located in the region of the aortic-pulmonary groove and over the pulmonary artery; posteriorly they are in the region of the aortic-auricular groove and on the posterior aspect of the aorta (Figs. 1, 2, and 7). As a matter of fact, the anastomoses are so abundant that the vasa of one coronary artery can be filled via the aortic branches of the other coronary artery (Fig. 3).

When accessory ostia of either the left or right coronary artery exist in the sinus of Valsalva, they are the chief origin of the aortic vasa (Fig. 4). It has been stated that the vessels of the dog's aorta arise predominantly from the right coronary artery in most animals.[3] However, our findings do not bear this out. Usually no predominance was found in our series except in those instances in which accessory ostia were present (Fig. 4). Actually we found:

No preponderance	45 dogs
Left preponderance	2 dogs
Right preponderance	3 dogs
Accessory ostia	7 dogs, in which there was a right accessory ostium and right preponderance in 5 dogs, and a left accessory ostium and and left preponderance in 2 dogs

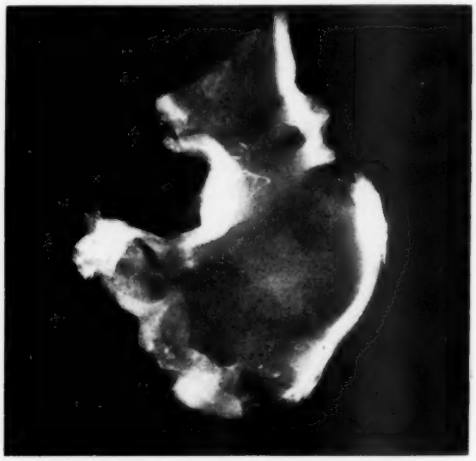

Fig. 5.—Arcuate branches of the left and right coronary artery supplying the root of the aorta and anastomosing with vasa of other origins. Note the direct vessel from the lumen of the aorta in the upper left-hand portion of the aorta.

Fig. 6—Direct vessel from the lumen of the aorta. Injection by aortic cannula in the arch with coronary arteries tied off at their orifice.

In addition to the vasa from the coronary arteries described, other vasa to the aorta arise more distally. These are the arcuate branches which supply the aorta and the aortic fat pad (Fig. 5). These arcuate branches anastomose freely with the other aortic vasa.

The other source for the adventitial network of the ascending aorta arises from the large arteries of the aortic arch and from the pericardium, descending

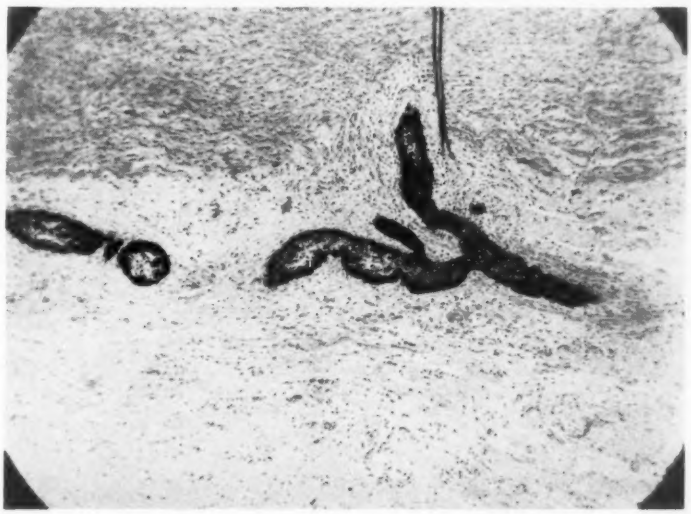

Fig. 7.—Anastomoses in the adventitia. Hematoxylin and eosin stain (× 56).

Fig. 8.—Ostium of a direct vessel from the lumen of the aorta filled with dye. Hematoxylin and eosin (×10).

from the pericardical reflexion. They anastomose extensively with the vasa arising from the coronary arteries as well as from the branches of the bronchial arteries which participate to a slight extent in the supply of the aortic wall near the bifurcation of the pulmonary artery.

Medial Network: The medial network is supplied by branches arising from the adventitial network and by vessels arising from the lumen of the aorta. The former is the more abundent source of supply.

Vasa from the adventita can be traced as far as the inner third of the media and anastomoses of these medial vessels can be seen in the outer and middle thirds of the media. The vascular supply of the media is not as rich as that of the adventitia (Fig. 7), and the extent of the anastomoses and the number of vasa decrease progressively in the media as the intima is approached. Medial anastomoses occur not only between branches arising from the adventitia but also between these adventitial branches and vessels arising directly from the lumen of the aorta.

Fig. 9.—Direct vessel from the lumen of the aorta which can be followed to the middle third of the media Hematoxylin and eosin stain (×67).

When the ascending aorta is opened, small lumina arising in the intima can be seen grossly; in injected specimens, they stand out as red points. These vessels can be followed and their branching traced in the x-ray pictures and in microscopic sections (Figs. 1, 5, and 8). The convincing demonstration that these vessels arise and are supplied from the lumen of the aorta was made in those experiments in which the dye was injected via an aortic cannula in the ascending

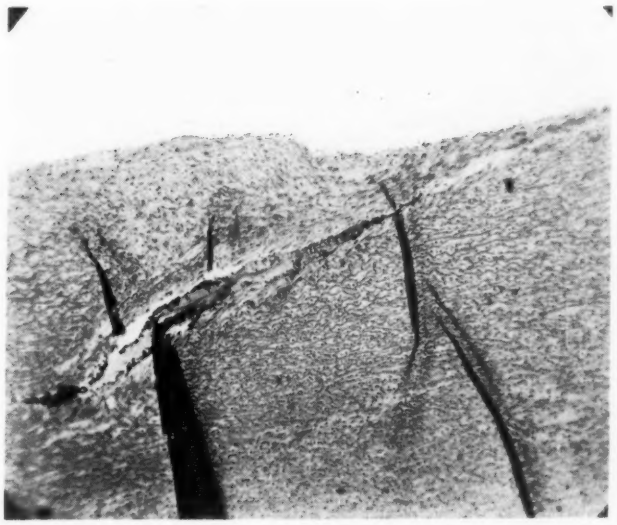

Fig. 10.—Direct vessel from the lumen of the aorta anastomosing in the middle third of the media with a vessel arising from adventitial network. Intima above. Hematoxylin and eosin stain (×56)

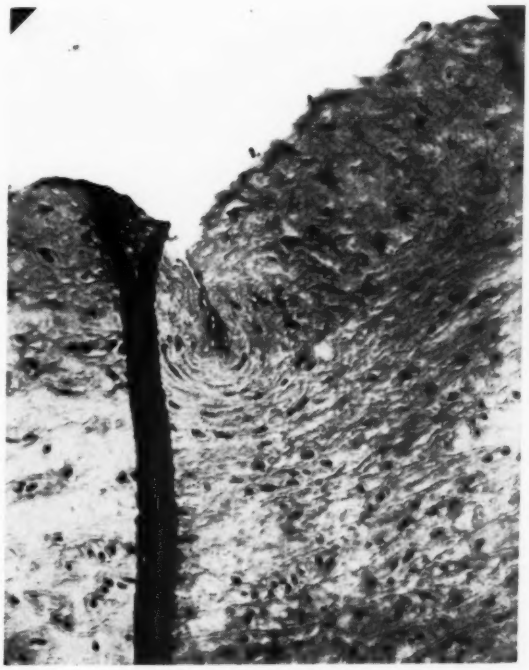

Fig. 11.—Stomas and small vessels below 10μ diameter arising directly from the lumen of aorta. Hemotoxylin and eosin stain (×204).

aorta facing upstream and in which the orifices of the coronary arteries had been completely occluded (Fig. 6).

Those vasa arising from the lumen of the aorta spread into the inner and middle third of the media and even reach its outer third and can be seen to anastomose with adventitial vessels (Figs. 9 and 10). On microscopic examination numerous small openings can be seen which are too small in diameter to be injected by the dye (Fig. 11). The larger vessels, 10μ or wider, arising directly from the lumen of the aorta, could not be found in the ascending aorta in dogs having accessory coronary ostia; however, the smaller stomas, below 10μ, were still demonstrable.

Arch and Descending Aorta.—Vessels arising directly from the lumen of the aorta and injectable by the dye used could be demonstrated also in the arch and descending aorta. These vasa and those arising from the large arteries of the aorta are the origin of the adventitial and medial plexuses of the arch and descending aorta. The adventitial plexus becomes progressively less extensive as one progresses from the ascending to the descending aorta. On the contrary the number of intimal vessels increases progressively along the downward course of the aorta.

DISCUSSION

The present study has demonstrated that there is an extensive and elaborate vascular supply to the aorta, richest in the ascending aorta. Its origin is from branches of the aorta, which give rise to an adventitial and a less extensive medial plexus, and from intimal vessels, many of which are more than 10 μ in diameter. As the adventitial plexus becomes less and less entensive in going downstream, the number of vessels arising from the intima increase, thus ensuring an adequate blood supply to the aortic wall.

The presence of vasa in the aortic wall had been demonstrated by Robertson.[3] Discreet openings in the lumen of the aorta were previously noted by Woodruff[4] in two dogs. Winternitz and co-workers[5] injected small stomas in the lumen of the aorta with India ink and found an intimal plexus by this means. However, it is not established that this India ink injected plexus constitutes a capillary vascular plexus. It may represent a network of intercellular spaces into which the highly diffusible India ink was forced by the injection method. When a coarser injection mass is employed, as in the present study, no intimal plexus can be demonstrated. The only vessels, of 10 μ or more, found in the intima were vessels running from the lumen to the media. The nourishment of the intima is thus dependent upon diffusion from the lumen of the aorta, from the medial vascular plexus, and from the scattered intimal vasa. Whether or not this is supplemented by a capillary network within the intima must remain undecided.

SUMMARY

1. The vascularity of the aorta in fifty-seven normal dogs was studied by an injection technique which disclosed the presence of vasa 10 μ or more in diameter.

2. An elaborate system of vasa was found consisting of an extensive adventitial plexus and a less extensive medial one.

3. These plexuses are supplied by vessels arising from the coronary arteries and the larger arteries originating from the arch of the aorta. In addition, vasa arising from the lumen of the aorta course through the intima to join the plexuses; the number of these aortic intimal vasa increases progressively caudad.

I am greatly indebted to Dr. Louis N. Katz for his guidance and suggestions during the progress of this investigation.

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Clinical Reports

RIGHT-SIDED AORTA WITH ATYPICAL COARCTATION INVOLVING ONLY THE LEFT SUBCLAVIAN ARTERY. HYPERTENSION

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THE case to be described concerned a young man, J. C. O., 22 years of age, Seaman, first class, in the Navy. He had been healthy all his life and indeed athletically inclined. At college he had played tackle on the freshman and varsity football teams. While attending a midshipman school in the Navy he was examined for promotion but was found physically unfit for a commission as ensign because of hypertension. On March 14, 1945, he was admitted to a U. S. Naval Hospital to appear before a board of medical survey for observation and report.

The young man was asymtomatic. Physical examination disclosed a person of unusually fine physique, who was tall and weighed 175 pounds. There were a few physical observations of note. Over the base of the heart a short systolic murmur was heard. The heart rate was slow, usually ranging from 45 to 60 beats per minute. The left radial pulse was definitely weaker than the right. In fact the pulsations in the brachial, axillary, and carotid arteries of the left upper extremity were smaller than the corresponding arteries of the right side. The blood pressure in the right arm was moderately but definitely elevated; the readings were 158-170/60-76. The pressures in the left arm were normal, 104-124/70-80. The definite abnormalities were therefore the small left radial pulse and the hypertension in the right arm.

The routine laboratory tests were not of significance. The Kahn was negative. Kidney function was excellent. An electrocardiogram disclosed a sinus bardycardia, the rate being about 42 beats per minute (Fig. 1).

The hypertension in an upper extremity, particularly in a young man, suggested the diagnosis of coarctation of the aorta. This diagnosis was dismissed, first, on clinical grounds and, second, by x-ray film of the chest. There was no abnormal relationship of the blood pressure in the upper and lower extremities,[1,2] no delay in rise or force of the femoral pulse, and no sign of collateral circulation in the chest wall, anteriorly or posteriorly, on inspection or by palpation. Nor did an x-ray film (Fig. 2) give any evidence of erosion of the ribs by dilated intercostal arteries serving as collateral circulation.

The blood pressure in the lower extremities was not decreased but presented the customary elevation above that obtained in the upper limbs. The right thigh arterial tension was 200/100 and the left femoral blood pressure was 200/90.

Pulse tracings of the right radial artery compared with that of either of the femoral arteries confirmed the clinical impression that there was no retarda-

The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

Received for publication Nov. 11, 1945.

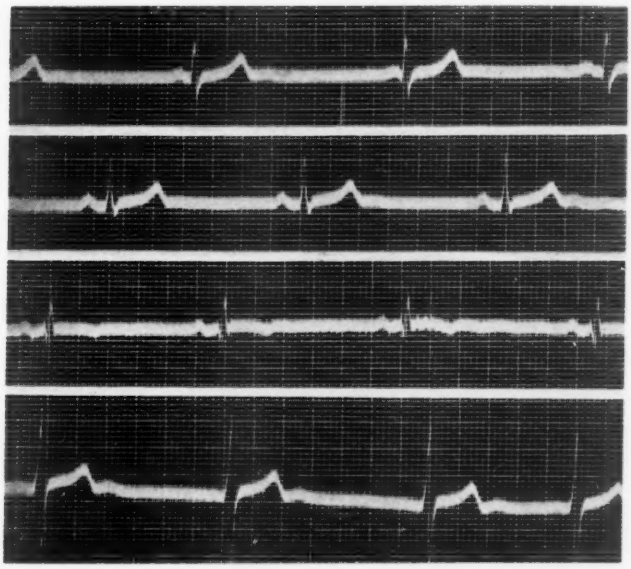

Fig. 1.—Electrocardiogram shows no abnormality. A sinus bradycardia is present; rate, about 45 beats per minute.

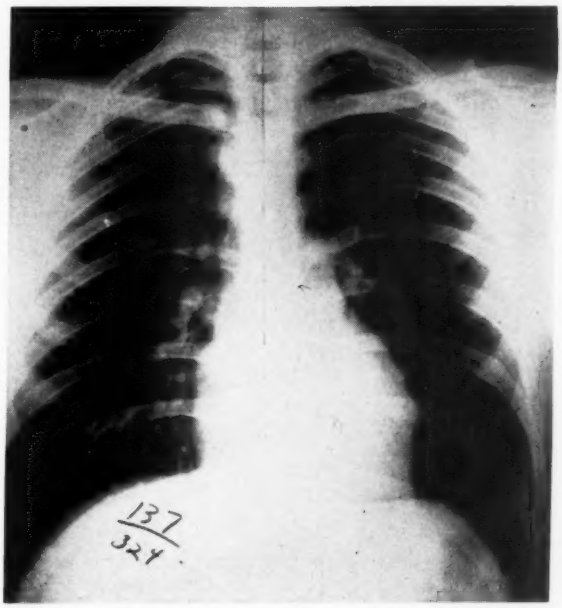

Fig. 2.—Teleroentgenogram reveals a normal globular-shaped heart. The aorta and aortic knob are on right side instead of on left.

tion of the pulses in the lower extremities. In typical coarctation of the aorta, Lewis[2] observed an average delay of 0.03 second in the pulse of the femoral artery.

The same teleroentgenogram of the chest which aided in disposing of the diagnosis of coarctation of the aorta disclosed a right-sided aorta (Figs. 2 and 3). The diagnosis of this congenital lesion was confirmed by fluoroscopy. The ingestion of the barium mixture revealed the esophagus, at the level of the aortic arch, to be displaced anteriorly and to the left of the aorta instead of being behind this structure (Fig. 3).

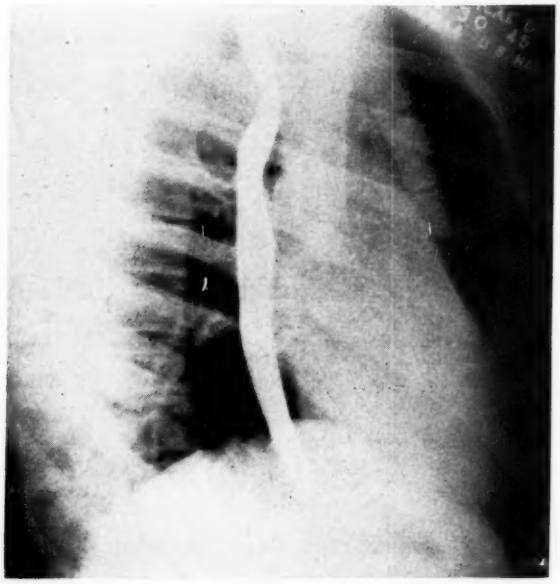

Fig. 3.—Lateral view film discloses barium-filled esophagus anterior to the arch of the aorta. Normally the esophagus is behind the aorta.

Although the diagnosis of right-sided aorta was definite, this still did not explain the *diminished left radial pulse* (Fig. 4) nor the hypertension in the right arm. To explain the small pulse in the left forearm a search was made for a left cervical rib. None was present in X-ray films of the chest. Nor was there any variation in the course of the left radial artery. The left upper extremity was completely normal in all other respects. The color and temperature were good. The grip of the left hand was just as powerful as that of the right.

We now considered two congenital anomalies of the left subclavian which could explain the decreased pulse of the left arm. A left subclavian artery has been known to originate on the right side in right-sided aorta and to be compressed in its long path to the left thorax.[1] Also a localized coarctation of the left subclavian artery, such as was recently described by Grishman, Sussman, and Steinberg,[3] would be as plausible an explanation. These investigators used the angiocardiographic technique which they have advanced so successfully. We therefore decided that diodrast injection would elucidate the problem. Several

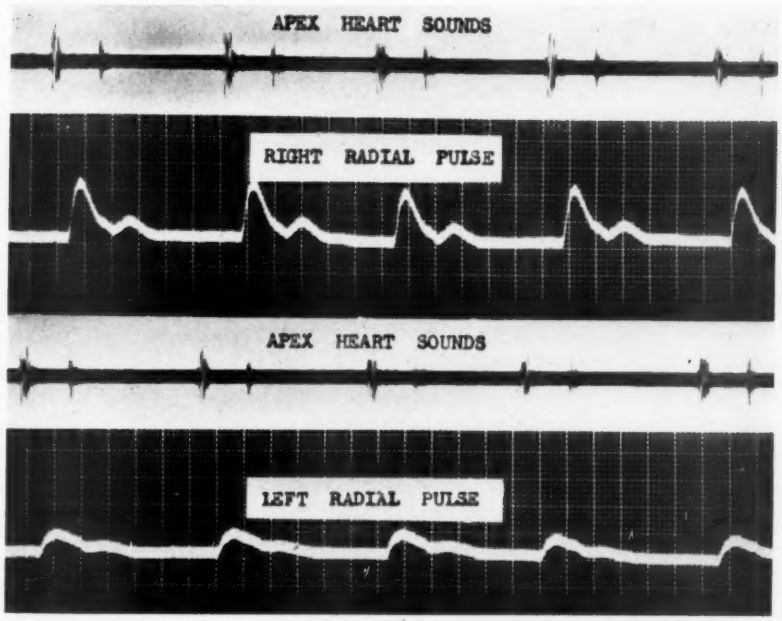

Fig. 4.—Phonocardiogram taken at the apex and pulse tracings of both radial arteries. The left pulse is distinctly smaller than the right and more gradual in its rise.

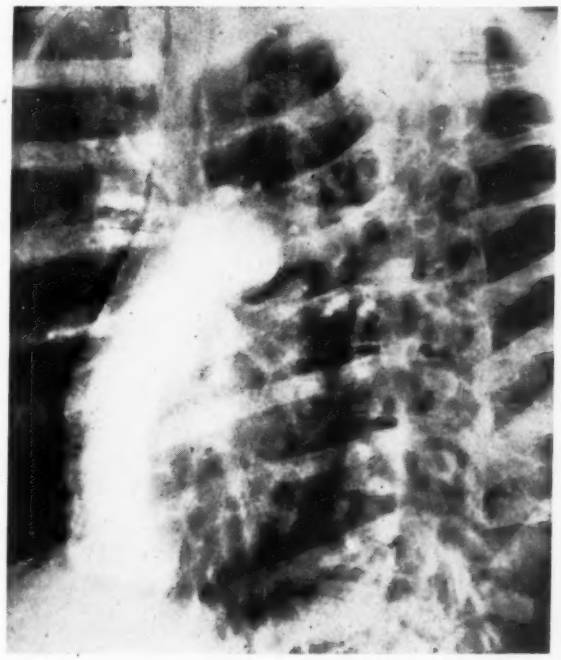

Fig. 5.—Angiocardiogram demonstrates a right ventricular filling with the diodrast substance passing valves of pulmonary artery. The septum is more convex than usual, probably indicating a hypertension in the left ventricle. (The cavity of this chamber appears to be increased in size.)

angiocardiographic studies were made.* In the first (Fig. 5), the diodrast is in the right ventricle and pulmonary artery. The latter is of normal size and its valves are visible. The cavity of the left ventricle which is not filled with diodrast appears to be increased in size and the ventricular septum appears to be more convex than usual, both of these findings being the result of the hypertension in the aorta.

Fig. 6 is an illustration of the opaque solution in the right ventricle, pulmonary artery, and the right and left branches of this vessel.

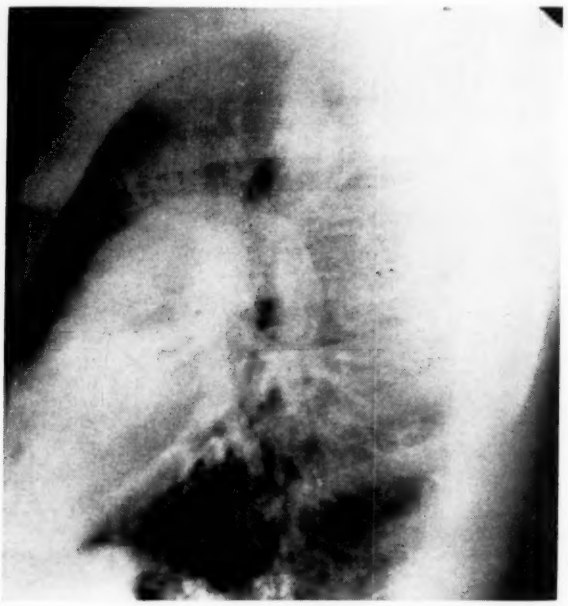

Fig. 6.—Angiocardiogram reveals the diodrast entering the left and right pulmonary arteries.

The final diodrast film (Fig. 7) shows the substance in the left ventricle and clearly in the aorta and in the right innominate and the left carotid arteries. There is no sign of the left subclavian artery. This latter vessel was atresic. The small left radial pulse was thus accounted for by a narrowed left subclavian artery. The aorta itself was normal in size and "measured 2.6 cm. in the suprasinus region, 2.5 cm. at the arch and about 2.1 cm. in the descending portion." There was no sign of hypoplasia or narrowing of the aorta such as Grishman and co-workers[3] discovered in their patients.

The final abnormality to be explained was the hypertension in the right arm. This was definite and had been present for some time. This conclusion was supported, first, by the examination of the fundus which disclosed slight indentation of the veins by the arteries where they crossed, and second, by the slightly

*Through the kindness of Dr. Marcy Sussman, the roentgenologist of the Mount Sinai Hospital, New York, N. Y., the angiocardiographic studies were made at that institution (Figs. 5, 6, and 7) and the films interpreted by him.

enlarged left ventricle and the displaced interventricular septum which had been forced to the right (Fig. 5).

The hypertension could be present in this patient as a coincidence, just as it is found not infrequently in so many other young men in the Armed Forces. A more plausible explanation is that the hypertension was associated with the coarctation of the left subclavian artery. In the three cases of localized coarctation of the left subclavian, described by Grishman and co-workers,[3] a hypertension in the right brachial artery was found in two patients.

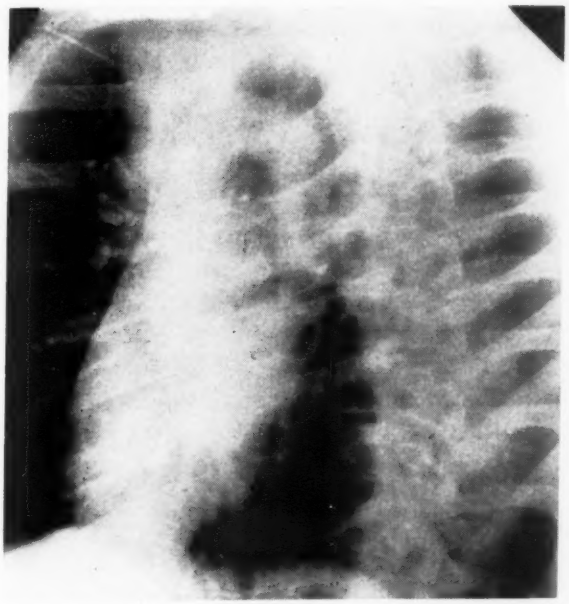

Fig. 7.—Angiocardiogram shows the diodrast in the aorta. White shadows are present where the right innominate and left common carotid arteries normally arise, but there is no evidence of a left subclavian artery.

COMMENT

Unequal radial pulses have been noted in coarctation of the aorta.[1,4] King[4, Table IV] cited nine case reports gathered from the literature in which the blood pressure in the right arm was definitely higher than that in the left. These patients may have possessed a coarctation of the left subclavian artery, but the aorta proper was narrowed since the blood pressure of the legs was lower than that of the arms. This is the discrepancy in blood pressure of the upper and lower extremities found in the ordinary case of coarctation of the aorta.

Grishman and associates[3] were the first to make a diagnosis of the atypical coarctation of the aorta with absence of left radial pulse by means of the diodrast method. Our case differs from theirs in that our patient revealed no extensive involvement of the aorta at the level of the isthmus and distal to the arch; the left radial pulse was not absent but was diminished in our patient; and, finally, a right-sided aorta was present.

Grishman and co-workers suggested that the diagnosis of atypical coarctation of the aorta may be suspected on clinical and polygraphic examinations but can be proved only by angiocardiographic study. We think that one should go further. We predict that a small or absent left radial pulse, with a hypertension in the right arm, but with the normal expected arterial tension in the femoral vessels, will often disclose a localized coarctation of the left subclavian artery. On the basis of the report by Grishman and co-workers, we suspected this diagnosis in our patient before the diodrast solution was used for confirmation.

When the left radial pulse is small or obliterated, other common conditions should first be thought of and eliminated before the diagnosis of coarctation of the left subclavian artery is hazarded. A large cervical rib is not uncommon. Many normal people can shrug their shoulders back and up and temporarily decrease, or totally obliterate, the radial pulse. Of course, in our patient the pulsation was permanently affected. A congenital anatomic variation in the course of the radial artery, an aortic aneurysm, or a tumor compressing the subclavian artery is to be considered before a diagnosis of coarctation of the left subclavian artery is made.

Hypertension is almost invariably present in typical coarctation of the aorta.[1,2] Steele[5] believes that not only is a systolic hypertension of the upper extremities present, but he maintains that the diastolic arterial tension in the lower extremities (and "inferentially the peripheral resistance") is often increased. He is of the opinion, therefore, that the hypertension in the typical coarctation of the aorta is a compensating mechanism to increase the general vascular tone in the whole body, lower extremities as well as upper. In our patient, then, the hypertension would simply be associated, perhaps reflexly, with the localized atresia of the left subclavian artery. It would be a systemic response of the arterioles to constriction of a large branch of the aorta.

The nerves in the carotid sinus and the arch of the aorta play an important role in controlling blood pressure. In a congenital malformation involving the aorta at the mouth of the subclavian, it is not illogical to expect an effect on arterial tension in the body, and seemingly this is always an elevation. The decrease in tension in the left arm was due to mechanical constriction of the left subclavian artery.

The bradycardia (heart rate, 42 beats per minute) may have been the slow pulse so often met with in athletes or it may have been produced by the nerve mechanism in the aorta in a way similar to that by which the hypertension was produced.

The absence of symptoms in this patient with both a right-sided aorta and a coarctation of the left subclavian artery is not surprising. The former congenital malformation is often discovered by accident. Lewis[2] studied the typical type of coarctation of the aorta in English Army veterans of World War I. He found that many had performed hard physical work for many years with no symptoms. In coarctation limited to the left subclavian artery, the arm undoubtedly receives a sufficient blood supply from collateral sources.

SUMMARY

A case has been described of right-sided aorta with coarctation of the left subclavian artery. The diagnosis was made clinically and by ordinary x-ray film and then confirmed by angiocardiographic films.

A small or absent left radial pulse in the presence of a hypertension in the right arm and a normal expected blood pressure in the lower extremities should lead to the consideration of the diagnosis of a localized coarctation of the left subclavian artery. Such causes as cervical rib, anomalous course of the left radial artery, tumors, and aortic aneurysm must first be investigated.

With a localized coarctation of the left subclavian artery, just as with the typical coarctation of the aorta, a hypertension is usually present. It is probably a reflex mechanism originating from the nerves in the aortic arch and producing an increased vascular tone in all the extremities.

Localized coarctation of the left subclavian artery frequently is discovered by accident. The patient presents no anatomic or physiologic defect in the left upper extremity except the small or absent left radial pulse. Hard work is quite compatible with the lesion.

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PAIN OF UNUSUAL DURATION DUE TO PROGRESSIVE CORONARY OCCLUSION WITH ASSOCIATED MEDIASTINAL TUMOR

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SCHENECTADY, N. Y.

ANGINA pectoris due to myocardial ischemia has been thoroughly studied by Keefer and Resnik.[1] They reviewed the former theories regarding this symptom complex and concluded that the coronary circulation became inadequate to meet various demands of the heart muscle when increased above its basal level. Lately, I have attended a patient who had steady, continuous, severe chest pain for eight days. He was unable to sit or lie down during this period. In either position, pain of an agonizing, tearing nature developed. Even while he was standing, some pain was present, but this was controlled somewhat by forty to sixty 1/100 gr. nitroglycerine tablets in the twenty-four hour period. The problem was complicated further by an unexplained tumor mass in the mediastinum between the posterior surface of the heart and the dorsal spine. This case is reported in detail because of the problem in diagnosis, the unusual fact that the patient was compelled by his pain to remain in the standing position continuously for eight days, and finally because of the finding at autopsy.

CASE REPORT

The patient was a 45-year-old man, whose weight was 200 pounds, height 5 feet 11½ inches; he had always been well up to twenty-two months prior to this illness. Previously the patient had been able to walk several miles with ease and had enjoyed hunting and fishing trips. The family history was negative: his father is alive and well at the age of 72; two older brothers have no history of heart disease; and his mother died of a cerebral accident at the age of 52.

The present illness began one year and ten months prior to death. At that time the patient was employed at heavy labor, lifting considerable weight during an eight-hour day. Gradually he noted the onset of substernal distress when lifting. During the course of the next few weeks a sense of pressure was present in the chest after a walk of three blocks at an average rate. He had a complete physical examination at this time, including gastrointestinal x-rays and an electrocardiogram. All studies were negative except the electrocardiogram, which showed low voltage T waves throughout with a definite cove T in the fourth lead (Fig. 1, *A*). He was advised that some myocardial damage was present, presumably on the basis of coronary sclerosis, given nitroglycerine for acute attacks of pain, and advised to keep his activities within the limits of the myocardial reserve. He gave up heavy work and secured employment of a light, sedentary nature. However, pain on walking continued, but this was promptly relieved by either rest or nitroglycerine. He continued in this state until early January, 1945, at which time he was referred to me for further study.

The essential findings at this time were a clear-cut history of angina on effort, an entirely negative physical examination except for a blood pressure reading of 174/110, a negative Wassermann, and an essentially normal electrocardiogram (Fig. 1, *B*). A comparison of this tracing with the one taken formerly (Fig. 1, *A*) shows improved voltage in the QRS complexes and all T waves. There are minor variations present, including more pronounced slurring of QRS_2 and some RS-T

From the Department of Cardiology, Ellis Hospital.
Received for publication Jan. 25, 1946.

segment changes in Lead IV F, but it was felt that minor deviations of this sort in a single tracing did not justify a definite diagnosis.[2] A repeated tracing (Fig. 1, *C*) was made immediately after the patient had exercised by the two-step method of Master.[3] This suggested temporary myocardial ischemia since it showed a depression of more than 0.5 mm. in the RS-T segment in Lead I and Lead IV F. The blood pressure and pulse rate had returned to their original levels within two minutes. After the last tracing was studied, the previous opinion of coronary artery disease was confirmed, similar advice offered, and enteric-coated aminophyiline, 3 gr. four times a day was ordered. The patient returned to his attending physician and was not seen again until five months later, thirty hours prior to death.

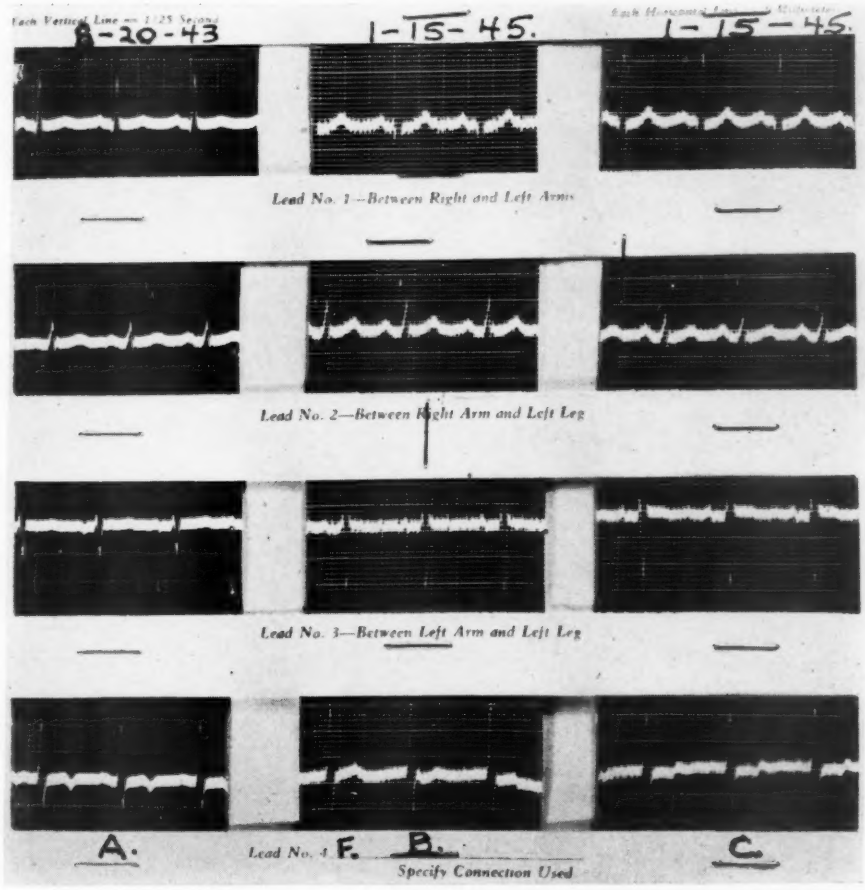

Fig. 1.—Electrocardiograms suggesting myocardial changes.

At this time the history obtained was that for the preceding week the patient had been unable to remain in any but a standing position. Liberal injections of morphine and atropine and papaverine by mouth as well as injection were of little help in controlling the pain. The only procedure of value was to allow the patient to stand upright and take from forty to sixty 1/100 gr. tablets of nitroglycerine during a twenty-four hour period. Although previous studies suggested that coronary insufficiency was present, it appeared questionable that this was the entire problem. Accordingly, the patient was hospitalized. Complete fluoroscopic and x-ray studies of the heart, mediastinum, lungs, esophagus, and great vessels were made. Two of these roentgenograms are

B.

A.

Fig. 2.—Roentgenograms of barium-filled esophagus showing tumor mass of uncertain etiology.

reproduced (Fig. 2). The report and conclusions of the roentgenologist* were as follows: Examination of the chest showed a symmetrical bony cage. The cardiac shadow generally was within the limits of normal in size, but there was a tumor mass projecting from the posterior surface of the heart, deflecting the esophagus posteriorly and to the right and producing a large central filling defect with no particular obstruction. The mass might have originated in the wall of the esophagus, but was not associated with the mucous lining. Impression: Mediastinal tumor or cardiac aneurysm.

Fig. 3.—Photograph showing tumor mass in the esophagus.

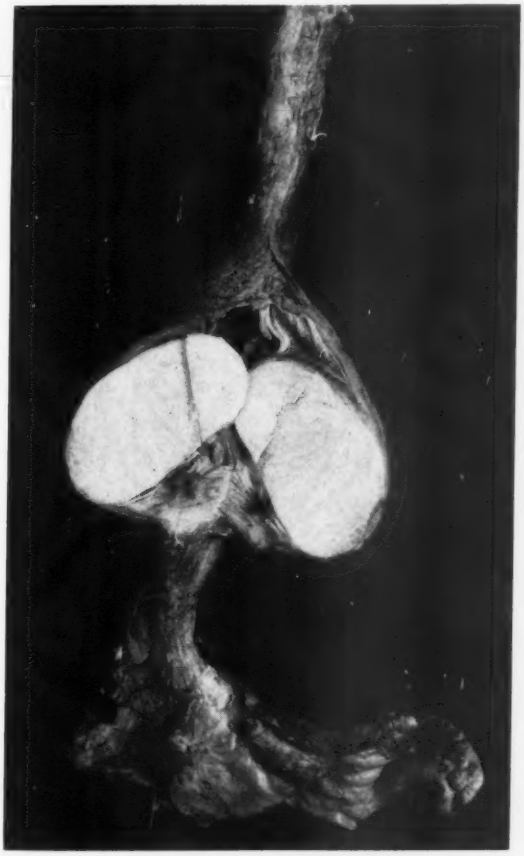

Fig. 4.—Photograph showing esophagus opened and split tumor mass in situ.

At the conclusion of the first and only possible series of x-rays, a careful esophagoscopy was considered for the following day. Meantime the patient secured enough relief from Demerol, 100 mg. intramuscularly every three hours, coupled with occasional injections of morphine ¼ gr., to permit him to sit in a chair for several hours and to obtain some degree of relaxation. There were no changes in the general physical examination except that the formerly elevated blood pressure was now 122/100. At no time during the illness was any digestive disturbance present. Unfortunately, due to technical difficulties, it was impossible to secure an electrocardiogram at this time. The patient was much more comfortable until ten minutes prior to death. He

*Dr. K. L. Mitton.

awakened suddenly and stood up, crying out with unendurable chest distress. The nurse left to get another hypodermic, but when she returned the patient had fallen to the floor and was dead.

Post-Mortem Examination.—Autopsy was performed twelve hours after death.* The essential gross findings reported were as follows: (1) Peritoneal cavity: The diaphragmatic domes were in the third and fourth innerspace on the right and left sides, respectively. The high position of the domes was apparently caused by the greatly enlarged liver. The serosal surfaces were

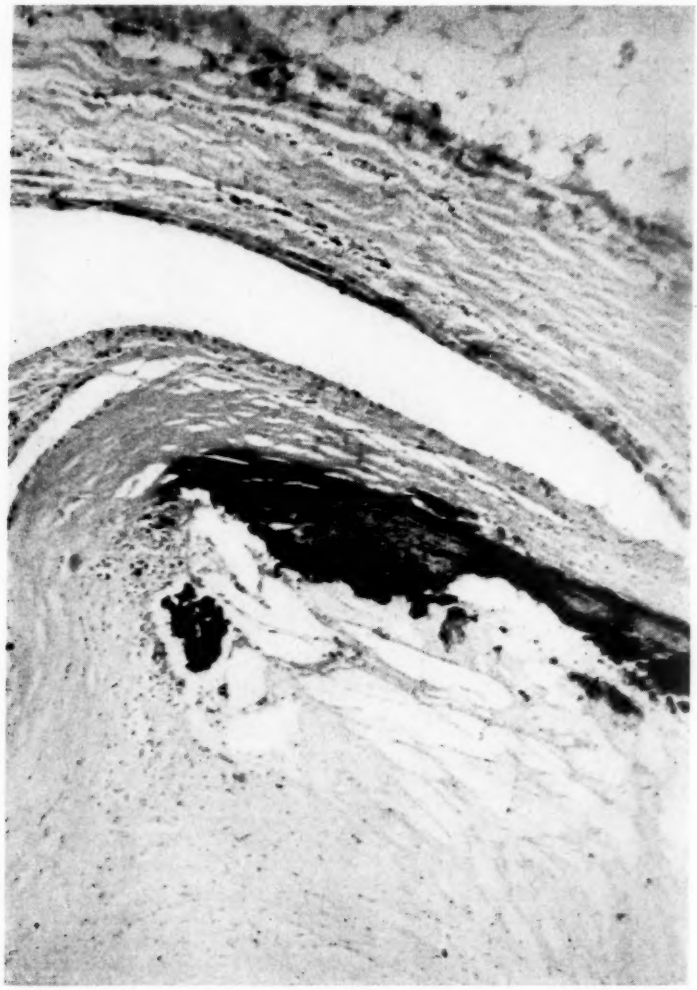

Fig. 5.—Photomicrograph (× 60) of large coronary artery showing organized, calcified thrombus.

smooth and shiny. (2) Heart: The pericardial cavity contained about 50 c.c. of straw-colored fluid. The heart weighed 400 grams. The epicardial fat was increased. The cavities were not dilated. The valves showed no lesions. The right ventricular wall was 4 mm. thick and flabby. The left ventricular wall was well contracted and had a diameter of 1.8 centimeters. Small foci of fibrosis were present in the interventricular septum. Both coronary arteries were tortuous

*Dr. M. Hirschfeldt Field, Pathologist.

and rigid. On cross section the walls were calcified and the lumen of the left descending coronary artery was of pin-point size 3 cm. from its origin. The right coronary was also calcified and the lumen was entirely obliterated 2 cm. from its origin. The smaller branches of the coronary arteries were patent. The ascending aorta, the arch, and the descending aorta showed a few elevated plaques in the intima but no calcification. (3) Mediastinum: A firm, oval tumor mass (Figs. 3 and 4) was palpated in the posterior mediastinum. On dissection it was found to arise in the wall of the esophagus. The tumor was well circumscribed 6 by 4.5 by 4 cm. and located

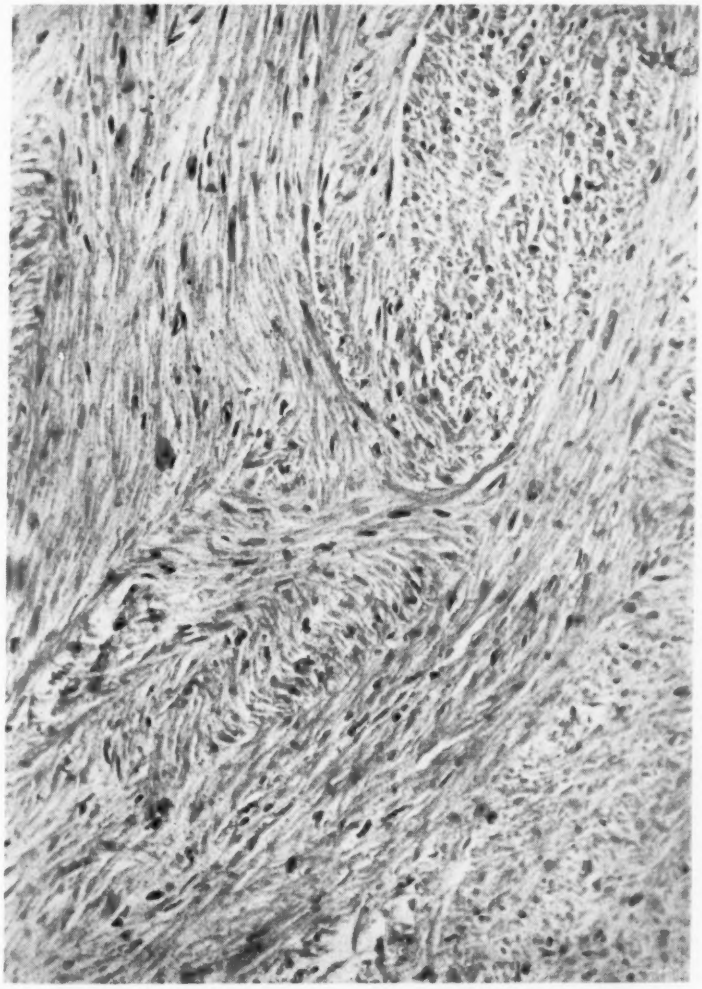

Fig. 6.—Photomicrograph (× 240) of the esophageal tumor showing leiomyoma of the esophagus.

5 cm. above the cardia. The lumen of the esophagus above the tumor showed no distention and there were no gross changes in the mucosa. The cut surface of the tumor was composed of grayish-white trabeculated tissue closely resembling leiomyoma. (4) Liver: The organ was markedly enlarged and weighed 2,700 grams. The left lobe extended to the left midclavicular line. The capsule was smooth. On section, the cut surface was brownish red, smooth, and resilient. The gall bladder and the bile ducts appeared normal. (5) Anatomical diagnoses: coronary sclerosis with complete occlusion of the right coronary artery and partial occlusion of the left descending artery; tumor of the esophagus; enlargement of the liver.

The essential microscopic findings reported were as follows: (1) Heart: Patchy areas were seen in which the muscle fibers were replaced by fibrous tissue. The nuclei in the muscle cell adjacent to these areas were enlarged and square. A large coronary vessel (Fig. 5) showed extensive calcification of the internal intimal layer and proliferation of the external intimal layer to such a degree that the lumen of the vessel was entirely obliterated. The adventitia showed no cellular infiltration. The changes in the aorta were minimal. There was some splitting of the muscle fibers and fat droplets were found in the cells. (2) Esophagus: Sections taken through the tumor (Fig. 6) showed the stratified squamous epithelium, the submucosa, and the nonstriated muscle layer to be normal. (3) Microscopic diagnoses: leiomyoma of the esophagus; fibrosis of myocardium; chronic passive congestion of liver.

DISCUSSION

The main point of the presentation meriting further discussion was the unexpected finding of a benign tumor of the esophagus associated with clinical coronary insufficiency. There was nothing in the history or physical examination to indicate any esophageal disease. The x-ray studies suggested a further possibility that a cardiac aneurysm rather than an esophageal tumor might be present. Although severe chest pain is seen frequently with myocardial infarction, its continuous presence for an eight-day period is most unusual. Occasionally, angina of rest or angina decubitis occurs, but even in these cases there are periods in which pain is absent or when active treatment will terminate this pain for a considerable period of time. It was the unusual presenting complaint of the terminal illness coupled with the unexpected finding of a mediastinal tumor that occasioned some doubt regarding the otherwise clear-cut diagnosis of progressive coronary insufficiency.

In a recent publication by Harper and Tisceno,[4] a review of the cases of benign tumor of the esophagus that have appeared in the radiologic literature was noted. They list fourteen, to which they add two cases of their own. Among the clinical symptoms summarized by them, one in particular may have some importance in conjunction with the case described here; namely, "Intermittent retrosternal sensation of dull pain or of pressure or of an 'aching sensation' which were usually referred to the lower or middle part of the sternum, being sometimes aggravated by lying on the back." Whether the tumor present in this case was a factor which prevented the patient from either sitting or lying down is open only to speculation. It has been found[5] that the general blood flow is greater in the recumbent position and thus the heart has more work to do than with the patient sitting or standing upright. It is possible in this instance that the myocardial reserve was so exhausted that standing may have been more economical from the standpoint of heart efficiency. Vinson,[6] in his monograph on The Diagnosis and Treatment of Diseases of the Esophagus, states: "Although benign tumors are not observed often, they occur frequently enough to require consideration in patients who present unusual symptoms referable to the esophagus. Myoma, which is the most common benign tumor of the esophagus, does not produce symptoms unless it attains considerable size. Diagnosis can rarely be made during life, but at many post-mortem examinations tumors of this type are noted." In a consideration of the diagnosis of this condition he

further states: "Roentgenoscopic study frequently reveals defects in the lumen of the esophagus, which may suggest the presence of a large tumor that does not cause obstruction to passage of a radio-opaque meal into the stomach. When such defects are noted, benign tumor should be suspected. In many cases diagnosis cannot be made without removal and microscopic study of the tumor during life or at post-mortem examination."

Thus it may be concluded that tumors of this type are not common and often cause no symptoms nor signs during the life of the patient. On the basis of these facts it is most likely that the clinical picture presented was due entirely to myocardial ischemia resulting from progressive coronary artery disease.

SUMMARY

This case is presented because of the unusual duration of chest pain, the fact that the patient had to stand upright for a continuous eight-day period, the extreme degree of coronary sclerosis with only suggestive electrocardiographic changes, as well as the difficulty added to the diagnostic problem by the presence of a mediastinal tumor of uncertain etiology. This is offered as a clear instance in which the importance of the history, when carefully taken and properly interpreted, is the deciding factor in the diagnosis of angina pectoris.

It is a pleasure to acknowledge the courtesy shown by Dr. Ellis Kellert, Ellis Hospital, in preparing pictures and photomicrographs of the tumor, as well as the kindness of Dr. H. Dunham Hunt, Saratoga Springs, N. Y., in furnishing the electrocardiogram reproduced in Fig. 1, *A*.

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COMPLETE AURICULOVENTRICULAR BLOCK AND BUNDLE BRANCH BLOCK WITH INTERCURRENT AURICULAR FLUTTER

REPORT OF A CASE
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CAMPINAS, BRAZIL

THE association of auricular flutter with complete A-V heart block was first demonstrated with electrocardiographic proof by Jolly and Ritchie in 1910[1] and is very uncommon. DiGregorio and Crawford[2] found only two instances in a series of 20,000 electrocardiograms. Willius[3] reported only one instance among 40,000 electrocardiograms. Up to 1939, only thirty-one cases had been reported in the literature and since then, additional reports have not increased the total beyond forty cases.

Among the reported cases of auricular flutter with complete A-V heart block, syphilis has been considered the most common etiologic factor, with rheumatic fever next in frequency; hyperthyroidism and congenital anomalies have been thought responsible for a small number of cases. Coronary sclerosis, however, should also receive etiologic consideration since a large proportion of the patients were over 50 years of age. Jourdonais and Mosenthal[4] have suggested a division of the cases into two types: (1) Patients who have both disturbances consistently and (2) patients who have one arrhythmia consistently and the other as a transient occurrence due to drug administration. Since it is frequently impossible to determine whether or not drug action is concerned, this classification seems rather unnecessary.

CASE REPORT

F. L. S., a 25-year-old man, was admitted to the Cardiological Service of the Irmãos Penteado Hospital on March 11, 1943, because of dyspnea on effort and at rest and edema of the face, abdomen, and legs. These symptoms had developed suddenly following ingestion of a vermifuge in January, 1943. From the first appearance of the symptoms, heart failure progressed gradually but steadily. Except for long-standing colitis, the patient had considered himself in good health prior to his present illness. His past medical history included epistaxis and "rheumatism" (apparently rheumatic fever) in childhood. He had several episodes of dysentery and frequent upper respiratory infections including pneumonia in 1941, at which date the sputum was negative for acid-fast bacilli. He had used alcohol moderately and had been active in sports, especially football. The family history was irrelevant.

Physical examination on admission to the hospital revealed a man of tall, slender build who was pale and orthopneic. The face, abdomen, and lower extremities were very edematous. The tonsils were hypertrophic. The teeth were carious. The thyroid gland was bilaterally enlarged. There were râles at both lung bases. The heart was greatly enlarged. The rhythm was irregular

From the Institute de Doenç as do Coração Dr. Pinto de Moura.
Received for publication Oct. 13, 1945.

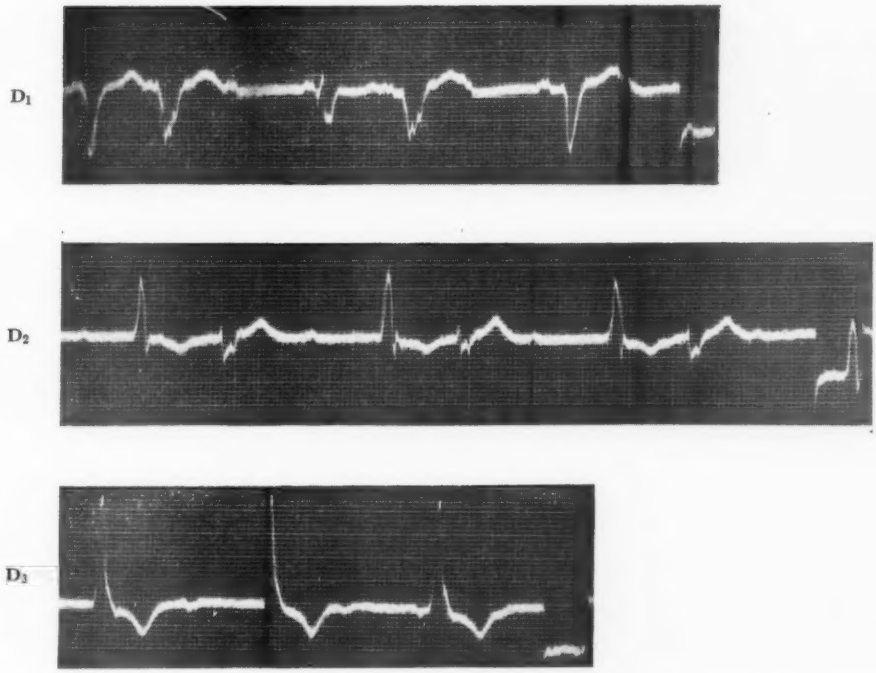

Fig. 1.—Electrocardiogram taken March 12, 1943, following admission to the hospital. Complete A-V heart block and right bundle branch block with ventricular extrasystoles.

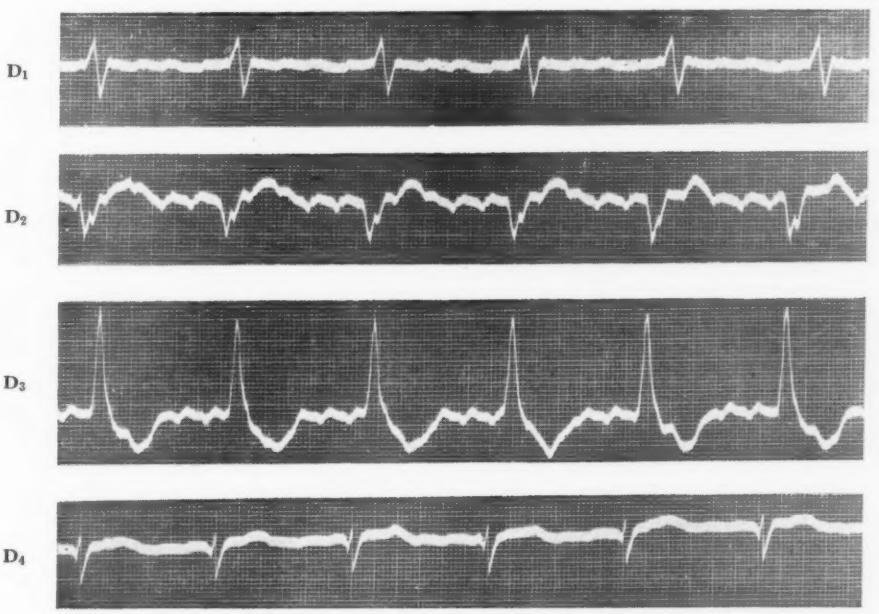

Fig. 2.—Electrocardiogram taken Aug. 4, 1944. Complete A-V heart block persists but auricular flutter has developed. The dominant ventricular complexes are now those which previously represented ventricular extrasystoles.

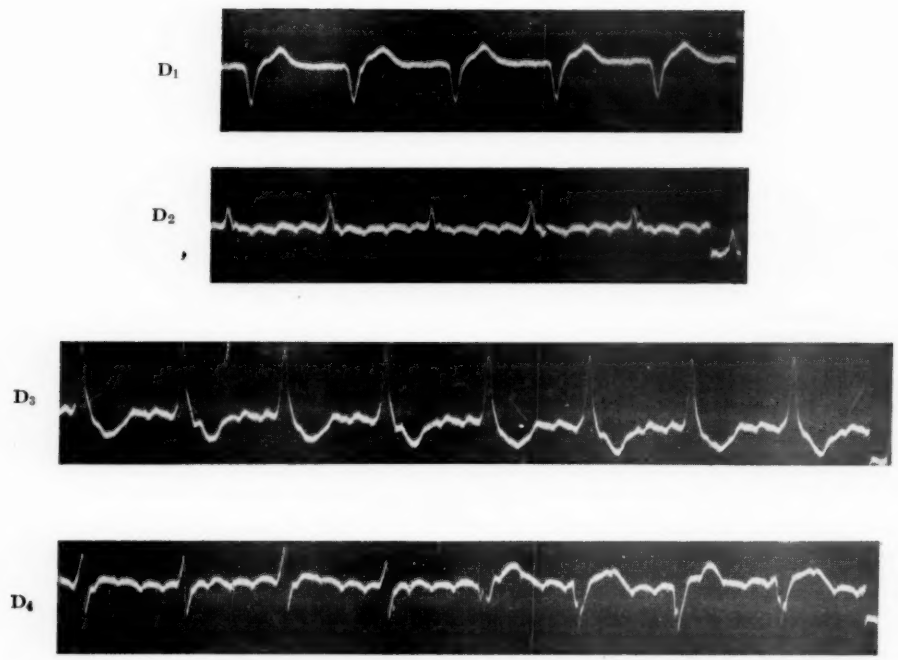

Fig. 3.—Electrocardiogram taken Aug. 5, 1944, following administration of digitalis. Complete A-V heart block and auricular flutter are present as on the preceding day (Fig. 2), but the dominant ventricular complexes are again those which were initially recorded (Fig. 1).

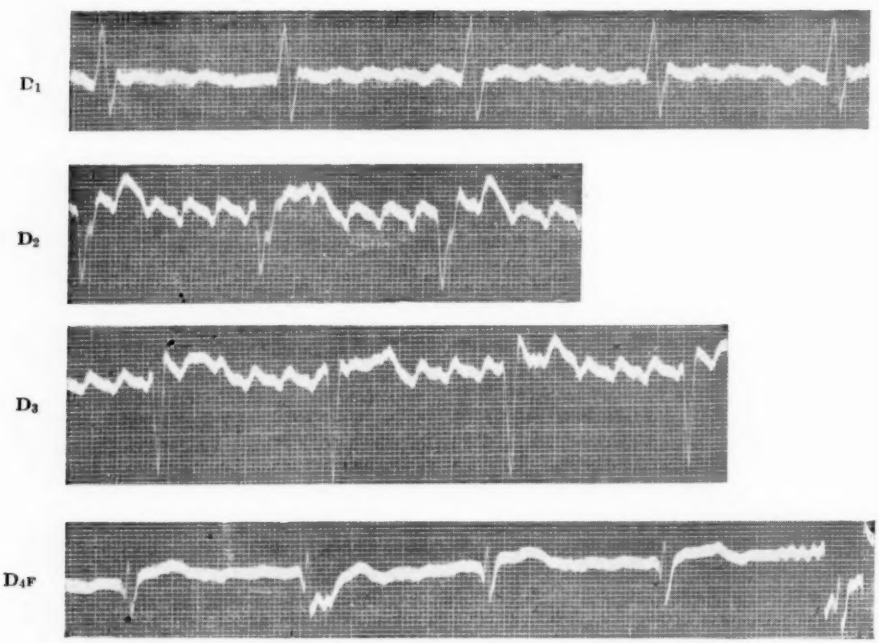

Fig. 4.—Electrocardiogram taken Sept. 27, 1944. Complete A-V heart block and auricular flutter persists, but the dominant beats have reverted to the type which were initially extrasystoles.

with a rate of 48 per minute. The heart sounds were diminished and a loud systolic murmur was audible over the entire precordium. Arterial pressure was 120/50. The liver was enlarged.

Routine laboratory studies showed a negative blood Wassermann reaction. The blood count was normal. Urinalysis was negative except for slight albuminuria. A phonocardiogram recorded a systolic murmur. An x-ray film of the chest revealed a greatly enlarged cardiac silhouette. The electrocardiogram (Fig. 1) showed complete A-V heart block with right bundle branch block and frequent ventricular extrasystoles.

The diagnosis was heart disease: (A) rheumatic fever, pneumonia (?); (B) cardiac enlargement, mitral insufficiency; (C) complete A-V heart block, right bundle branch block, ventricular extrasystoles, congestive heart failure; (D) Class IV.

The patient was confined to bed and treatment included the administration of Salyrgan and of Deriphyllin in 50 per cent glucose solution intravenously. Improvement followed and the patient was soon able to be out of bed. From time to time he left the hospital without permission and attempted to work but was soon forced to return because of aggravation of his symptoms. In August, 1944, following such an absence, an electrocardiogram was made which showed auricular flutter (Fig. 2). It is noteworthy that the complexes which had previously represented the premature beats now constituted the dominant beats. Digitalis was then administered, following which the electrocardiogram (Fig. 3) showed a reversion of the ventricular complexes to the type which had been dominant prior to the onset of auricular flutter. The next electrocardiogram, made in September, 1944, showed that once again the beats which originally had been ectopic had become the dominant type (Fig. 4). No change was present in the last electrocardiogram made in November, 1944.

In December, 1944, heart failure recurred in severe form and progressed in spite of further treatment with digitalis and salyrgan. Death occurred suddenly. There was no opportunity for terminal observations.

DISCUSSION

As previously mentioned, the association of complete A-V heart block with auricular flutter is extremely rare. The present case is presented because of the exceptional association of four defects: complete A-V heart block, bundle branch block, coupled extrasystoles, and auricular flutter. It appears that the rheumatic process affected the conduction system, cicatrization of which produced first the A-V heart block and then the bundle branch block. The extrasystoles could be explained by the necessity for a pacemaker in the lower center. Drug action was not responsible for these phenomena for quinidine was withheld because of the possibility of producing embolism and digitalis was given only in relatively small dosage. Because of the extent of the organic myocardial damage, treatment could be expected to bring about little more than subjective improvement. Such actually was the case and the progress of the disease continued almost uninterruptedly to its fatal termination.

SUMMARY

A case of complete A-V heart block associated with bundle branch block, ventricular extrasystoles, and auricular flutter is reported. This combination of defects is very rare. The apparent etiologic factor was rheumatic fever which caused an unusual degree of damage to the conduction system. The patient was observed over a period of seventeen months; he died of sudden acute heart failure.

The author wishes to express his appreciation to his assistant, Mrs. Ruth Szyszka, for her valuable assistance.

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Abstracts and Reviews

Selected Abstracts

Stein, L., and Wertheimer, E.: Cardiac Metabolism and Rigor in Thyroidectomized Rats. Arch. internat. de pharmacodyn. et de thérap. **71**:129 (Nov.), 1945.

The fact that cardiac rigor develops more slowly in thyroidectomized than in normal rats prompted an investigation of some of the conditions upon which the course of the cardiac rigor curve depends. The studies were made on rats which had been fed a standard carbohydrate diet. The hearts were removed from the living animals in sixty to ninety seconds, suspended in a Ringer bath, and attached to a kymograph for recording their movement.

It was found that the heart produces a normal rigor curve only when it is isolated while the animal is under deep narcosis. A shock type of rigor curve, brief in duration, occurs when the heart is removed after the rats are rendered unconscious by a blow on the head. Previous treatment with caffeine or strychnine, as well as acute asphyxia or poisoning with KCN, produces a similar result. Fatigue and exhaustion or thyrotoxic influence cause a marked curtailment of the rigor curve. Digitals or cardiazol almost completely nullifies the effect of brain shock, asphyxia, or exhaustion on the rigor curve but do not nullify the influence of the thyrotoxic principle.

The cardiac rigor curve of thyroidectomized rats is essentially different from that of normal rats. It is of greater duration and is not influenced by brain shock, caffeine, strychnine, exhaustion, or digitalis. Acute asphyxia has less influence than it has on the curve of normal rats. Chemical rigor produced by mono-iodoacetate poisoning is essentially the same in thyroidectomized rats as in normal rats. The duration of rhythmic contraction of the thyroidectomized rat heart in Ringer solution is twice that of the normal rat heart. LAPLACE.

Heymans, C., Casier, H., and Delaunois, A. L.: The Influence of Alcoholemia on the Proprioceptive Reflexes for the Regulation of Arterial Pressure. Arch. internat. de pharmacodyn. et de thérap. **71**:103 (Nov.), 1945.

Intoxication by ethyl or methyl alcohol depresses the central nervous system and favors the occurrence of a state of shock, especially post-traumatic cardiovascular collapse. A further study of the subject was made to determine the effect of alcohol on the aortic and carotid sinus reflexes because these are the mechanisms which regulate and maintain the normal arterial pressure, and their suppression predisposes to cardiovascular collapse.

The experiments were performed on dogs which had been anesthetized with chloralosane and were given artificial respiration. In order to limit the proprioceptive regulation of blood pressure to the carotid sinus reflexes, the cervical vagus-aortic nerves were sectioned. The capacity of the animal to react against circulatory collapse was determined by occluding the two common carotid arteries. When the normal compensatory reactions had been determined, a 25 per cent solution of alcohol in isotonic serum was administered intravenously and the intensity of the vaso-hypertensive reflexes of the carotid sinus was recorded at regular intervals.

The results obtained indicate that: (1) weak doses of ethyl alcohol are capable, in the first phase, of stimulating the vaso-hypertensive reflexes of the proprioceptive arterial pressure regulating mechanism; (2) the proprioceptive reflexes of the carotid sinus may suddenly become completely suppressed when the blood alcohol concentration reaches 0.2 to 0.4 per cent (this depressant action predisposes to cardiovascular collapse); (3) the reflexes concerned in the automatic regulation

of arterial pressure are rapidly restored in proportion to the decline of blood alcohol level; (4) intoxication with methyl alcohol produces a similar but more prolonged effect.

LAPLACE.

Movin, R., Ohlsen, A. S., and Pedersen, A. M.: Arterial Hypertension—Nephrectomy. Acta med. Scandinav. **119**:439 (VI), 1944.

A 6-year-old boy with a history of hematuria and pyuria since the age of 18 months and of increasingly severe headaches for two years was found to have a blood pressure of 170/120. There was no function of his right kidney; the left kidney was apparently normal. The eye grounds and the electrocardiogram were normal.

An attempt at right pyelography was followed in six hours by a severe hypertensive encephalopathy, with three hours of convulsions and coma. Two other encephalopathic episodes occurred spontaneously during the ensuing three weeks.

The systolic blood pressure fell to below 100 one hour after right nephrectomy was performed. After thirty-six hours of severe oliguria with the blood urea nitrogen rising to 100 mg. per 100 ml. the boy recovered completely. He was followed for eighteen months, during which period no abnormalities of blood pressure or renal function were detectable.

The right kidney was the seat of severe chronic pyelonephritis with marked thickening of the capsule and atrophy of the renal parenchyma. Microscopically the arterioles were greatly narrowed and showed marked thickening of their intimal and medial coats but no necrosis.

The authors believe their case demonstrates that excellent results may be expected from nephrectomy when hypertension, caused by unilateral renal disease, has not yet resulted in significant damage to the opposite kidney or to the cardiovascular system. SAŸEN.

Duancic, VI.: On the "Paradoxic" Action of the Sympathetic and the Vagus on the Coronary Arteries. Ztschr. f. Kreislaufforsch. **34**:99 (No. 3), 1942.

The author cites and believes he has confirmed previous reports in the literature that the media of the coronary arteries contains a much larger proportion of spiral fibers than other arteries. The action of spiral fibers is to shorten the vessel and thus enlarge the lumen, producing effects opposite to that of circular fibers. Likewise, relaxation of spiral fibers results in lengthening of the vessel and in a smaller lumen. A similar situation is said to exist in the bronchial tree of human beings (Ztschr. f. Kreislaufforsch. **34**:21 (No. 1), 1942). Human coronary arteries have, in addition, a well-developed longitudinal muscle layer which has an action similar to that of the spiral fibers. It is proposed that in all vessels the contraction of arterial and arteriolar muscle coats results from sympathetic stimulation but that the effect of such contraction is opposite in the coronaries, since the lumen is enlarged through shortening of the vessel length. The results of parasympathetic stimulation are opposite. Thus the postulation of a different muscle reaction in coronary vessels (and the human bronchial tree) from that resulting in other arteries in the organism would be unnecessary. SAŸEN.

Huntington, R. W., Ryan, R. D., Butt, H. R., Griffiths, G. C., Montgomery, H., Solley, R. F., and Leake, W. R.: Studies in Rheumatic Fever: II. Absorption of Salicylates. Ann. Int. Med. **24**:1029 (June), 1946.

This report deals with observations made among a group of patients with rheumatic fever in whom treatment consisted of large doses of salicylates administered by the oral, rectal, and intravenous routes. The comparisons were made between the administration of sodium salicylate and of acetyl salicylate. This medication was given with and without sodium bicarbonate. On the basis of serum salicylate levels it was concluded that salicylate is readily absorbed from the upper end of the gastrointestinal tract but is poorly absorbed from the lower end. For this reason the authors recommend that salicylate should never be given in enteric-coated tablets or by rectum. They also suggest that the gastric irritation resulting from the administration of the ordinary tablets of sodium salicylate by mouth can be minimized by the simultaneous administration of

food or bicarbonate. In their experience, bicarbonate sufficient for this purpose (60 gr. daily) should not cause a definite reduction in the serum salicylate level. They also found that the concomitant administration of bicarbonate did not reduce the blood level of salicylate below what would ordinarily occur without the bicarbonate. They also stressed the fact that there is practically no need for resorting to intravenous salicylate administration inasmuch as adequate blood levels can be achieved by giving the drug by mouth.

WENDKOS.

Fagin, I. G., and Schwab, E. H.: Spontaneous Mediastinal Emphysema. Ann. Int. Med. **24**:1052 (June), 1946.

In this article the authors describe three new cases of mediastinal emphysema and review all previously published cases. The differentiation of this condition from true cardiac disease, such as acute myocardial infarction, acute pericarditis, dissecting aortic aneurysm, and pulmonary embolism is stressed. In this regard, the absence of significant electrocardiographic changes as a diagnostic feature of mediastinal emphysema is emphasized. The proper use of the roentgenogram as a diagnostic aid is demonstrated. The frequent association of pneumothorax is also pointed out and its mechanism is briefly discussed. The benign and self-limited nature of spontaneous mediastinal emphysema is reaffirmed. There is an adequate discussion of mediastinal crepitation (Hamman's sign) as a diagnostic feature. Included are reproductions of sound tracings which show how the acoustic qualities of mediastinal crepitation differ from those of a pericardial friction rub.

WENDKOS.

Moberg, G.: Intravascular and Extravascular Pressure in Valsalva's Experiment. Acta radiol. **27**: 392 (No. 3-4), 1946.

The validity of Westermark's method of measuring pulmonary artery pressure by holding the breath against a measured pressure which diminishes the size of the pulmonic vascular shadows is questioned. The author believes that this or any modification of the Valsalva experiment would have a selective effect on the pulmonary arterial circulation only if the chest were open and the lung inflated by the intratracheal pressure. The Valsalva experiment is asserted to convert the whole of the abdomen and thorax into a chamber in which there is a relatively uniform increase of pressure which would act on the great vessels and the right ventricle equally with the pulmonary capillaries except for the elastic recoil of the lungs. This results in the blood being forced from the trunk into the extremities, head, and neck. The diminution in size of vascular shadows would thus be due to a smaller amount of blood in vessels of widely varying size and pressure and not to an effect on the pulmonary vascular bed alone and would therefore have no significant relation to the pulmonary arterial pressure.

SAYEN.

Laquime, J., and van Heerswynghels, J.: A New Classification of Congenital Cardiopathies. Acta med. Scandinav. **118**: 244 (No. 1-3), 1944.

A classification is suggested based on the presence or absence and the type of vascular shunt between the greater and lesser circulations in congenital heart disease. This would avoid the use of cyanosis as a criterion as was done by Abbott. The difficulties involved in evaluating the multiplicity of factors affecting cyanosis are detailed. The authors suggest cases be grouped as follows:

1. Those with no vascular shunt.
2. Those with a shunt, which may be of two types:

(A) Arteriovenous shunts, evidenced by reduction in carbon dioxide tension in the pulmonary arterial blood which can be measured by rebreathing various mixtures of a gas and obtaining equilibrium. This group would include interventricular and aortic septal defects, patent atrial septum, patent ductus arteriosus, and transposition with septal defect.

(B) Venoarterial shunts, determined by studying arterial unsaturation in the systemic circulation. This group would include the tetralogies of Fallot and Eisenmenger, cor biloculare, and other similar defects.

SAYEN.

Brummer, D.: Proteinuria of Effort and Its Significance in the Diagnosis of Congestive Heart Failure. Acta med. Scandinav. **124:** 252 (No. 3), 1946.

The author believes that the concept of "physiologic" proteinuria up to 2.0 to 8.0 mg. per cent, which is based on the work of Mörner (1895), is incorrect. The usual clinical tests for albuminuria are relatively inaccurate and are negative unless a proteinuria of at least 5.0 to 10.0 mg. per cent is present. Using precipitation by salicylsulfonic acid and a set of dilute solutions of precipitated serum as comparators, proteinurias of less than 1.0 mg. per cent can be measured. Of 50 "normal" patients, none showed more than 1.0 mg. per cent of protein at rest; exercise (forty knee bends) did not increase this significantly. Twenty-five of thirty patients with acute febrile diseases had 1.4 to 7.1 mg. per cent of proteinuria, whereas only 40 per cent of the group showed a positive albumin test by routine methods. Patients with acute glomerulonephritis or acute pyelonephritis showed increased proteinuria after exericse. Those with chronic renal disease did not.

Nineteen cardiac patients without failure showed no increase above the author's strict normal standards at rest or after exercise. Of thirteen patients with congestive failure, exercise produced significant increases of protein above their normal resting figures in patients with mild signs of congestion. Patients with more severe congestion had abnormal proteinuria at rest and a further considerable increase after exercise. This occurred with left-sided failure and not necessarily only when venous pressure was elevated. There was no quantitative relationship between the amount of proteinuria and the severity of congestive failure. In the absence of acute renal or febrile systemic disease, a resting proteinuria greater than 1.0 mg. per cent and a postexertional proteinuria greater than 2.0 mg. per cent in cardiac patients is felt to be evidence of congestive heart failure.

SAŸEN.

Scherf, D., and Schlachman, M.: The Effect of Methylxanthines on the Prothrombin Time and the Coagulation of the Blood. Am. J. M. Sc. **212:** 83 (July), 1946.

The investigations reported show that there is a definite shortening of the prothrombin time and of the plasma coagulation time following an intravenous injection of aminophylline. The changes were often found within one hour after the injection, reached a maximum four to five hours later, and often persisted after twenty-four hours. Since the intravenous injection of theophylline with sodium acetate had a similar effect, the action is not bound to the ethylenediamine which is used as a solvent for the theophylline. The oral administration of methylxanthines was likewise found to shorten the prothrombin and plasma coagulation times. The possibility is suggested that the increased coagulability of the blood may augment the danger of venous thrombosis in the bedridden patient or the risk of coronary thrombosis in a patient with coronary sclerosis.

On the other hand, it is suggested that the methylxanthines may be of value as styptic agents in hemorrhagic disease. The cause of the hyperprothrombinemia produced by these drugs is unknown, but a functional stimulation of the hepatic tissue has been suggested as a causative factor.

DURANT.

De Takats, G., Fowler, E. F., Jordan, P., and Risley, T. C.: Sympathectomy in Peripheral Vascular Sclerosis. J. A. M. A. **131:** 495 (June 8), 1946.

These authors discuss their experiences in using sympathectomy for the treatment of peripheral vascular sclerosis of the lower extremities. The indications for sympathectomy were as follows: patients with popliteal, femoral, or aortic occlusions who showed a favorable response to paravertebral block with procaine and whose visceral vascular involvement was subclinical or slight (no hemiplegia, no coronary occlusion, no advanced nephrosclerosis); patients with or without diabetes whose chief complaint was continuous intractable burning pain associated with osteoporosis, who obtained relief from paravertebral block and who otherwise would require a supracondylar amputation (a causalgic state). The age group between 40 and 50 was found to be most favorable.

The material consisted of twenty-five patients ranging in age from 39 to 66 years who were placed in the vascular sclerotic category because of (1) definite evidence of sclerosis elsewhere; (2) absence of a history of segmental phlebitis or arteritis in earlier years and no involvement of radial arteries; (3) high pulse pressure, hypertension, hypercholesteremia, or hyperglycemia.

The following results were obtained. Group I included nine middle-aged sclerotic patients with a previous walking ability limited to a few blocks. These patients were greatly benefited by lumbar sympathectomy: their walking ability improved, occasionally for unlimited distances; in two patients it improved to a point where they developed angina of effort. Group II was made up of patients whose walking ability ranged from one-half to two blocks. Operation was undertaken mainly to prevent gangrene. Not a single patient developed gangrene on the sympathectomized side; two patients lost their legs on the side not operated upon, which were originally the better legs. Group III included patients requiring amputation or who had already lost one leg by amputation. As a result of lumbar sympathectomy the authors were enabled to do three toe amputations and three lower leg amputations in the presence of a type of circulation which their previous experience indicated would have necessitated a supracondylar amputation. The patients in Group IV had intractable pain, diffuse osteoporosis, and glossy edema. These patients were regarded by the author as belonging to the casualgic state. These patients also showed improvement after sympathectomy.

BELLET.

Leevy, C. M., Strazza, J. A., Jaffin, A. E.: Fluids in Heart Failure. J.A.M.A. **131:** 1120 (Aug. 3), 1946.

One hundred twenty-two patients with congestive heart failure were studied to evaluate the relative merits of restriction of fluid intake, allowing fluids ad libitum, and forcing fluids.

Currently, most clinicians allow only 1,000 to 1,500 c.c. of fluids daily as an integral part of their cardiac regimen in treating congestive heart failure. They feel that more may increase the burden on the heart. Members of the ad libitum school feel that limiting or forcing fluids may may prove difficult, hazardous, or uncomfortable, whereas champions of the forcing-fluids school of thought believe that with the ever-present renal function impairment in cardiac decompensation, more water than normal is necessary to eliminate normal waste products without having the kidney work at maximum capacity.

All patients admitted to the general medical service with congestive heart failure were divided into three groups: Group I consisted of thirty-six patients on a restricted fluid regimen of 1,200 c.c. daily; Group II was composed of forty-eight patients placed on a fluids ad libitum regimen; Group III included thirty-eight patients who received a minimum daily fluid intake of 3,000 cubic centimeters. All patients were placed upon the same fundamental cardiac regimen, the only essential difference being the amount of fluid intake. Patients were given an acid ash, salt poor diet which provided sufficient calories, proteins, minerals, and vitamins, and at the same time insured a low sodium intake, low salt intake, and an acid ash.

The following results were noted: In the group permitted to drink fluids ad libitum, the average cardiac patient consumed approximately 1,700 c.c. of water daily in the summer and only 1,300 c.c. in the winter. Patients allowed to drink water as they desired were much more comfortable than members of the other groups. In no instance was increased intake associated with evidences of the circulation becoming overburdened, increase of decompensation, or water intoxication.

Of the thirty-eight patients on a forced-fluid regimen with a minimum daily intake of 3,000 c.c., seven (18.3 per cent) became nauseated and were compelled to discontinue the treatment. Of those adhering to forced fluids, twenty-seven felt greatly improved. The average amount of fluid consumed daily by the individuals of this group was 5,750 cubic centimeters. In no instance did pulmonary edema or hypertensive encephalopathy incident to cerebral edema follow the regimen of forced fluids.

Of thirty-six patients in whom fluids were restricted, 27.7 per cent complained of thirst (52.6 per cent of those observed during summer and 47.4 per cent during winter); 13.6 per cent of patients discontinued restriction because of thirst. Restricted fluids may lead to dehydration with disorientation.

These authors conclude that with restricted sodium intake, restriction of water is unecessary in treating cardiac decompensation—that restriction of fluids increases the discomfort of the patient and may prove deleterious. In most decompensated cardiac patients, forcing fluids will neither retard nor facilitate compensation. The average patient with congestive heart failure should be allowed to drink water as it is desired and should consume enough to maintain a daily minimum urinary output. When congestive heart failure is complicated by sepsis, fluids should be forced to obtain optimum therapeutic results. Likewise, water intake should be increased to prevent dehydration where there is intrinsically impaired renal function or excessive skin or urinary water loss.

BELLET.

Levy, R. L., White, P. D., Stroud, W. D., and Hillman, C. C.: Overweight: Its Prognostic Significance in Relation to Hypertension and Cardiovascular Renal Disease. J. A. M. A. **131:** 951 (July 20), 1946.

A statistical analysis was made of the medical records of 22,741 officers in the United States Army to determine the prognostic significance of overweight noted in the course of annual physical examinations.

An officer was considered to be overweight when he was heavier, by twenty pounds (nine kilograms) or more, than the standard given in army regulations, calculated according to height and age. By sustained hypertension was meant a reading of over 150 systolic or 90 diastolic persisting throughout one examination and not followed in subsequent examinations by lower levels.

When the combination of overweight, transient hypertension, and transient tachycardia was present, the probability of the later development of sustained hypertension was twelve times as great as in normal controls. In the case of retirement with cardiovascular renal diseases, the probability was four times as great. Overweight alone did not increase significantly the death rate from cardiovascular renal diseases. Transient hypertension or transient tachycardia or overweight by itself increases the probability of the later development of sustained hypertension and of cardiovascular renal disease.

BELLET.

Iandolo, C., and De Rysky, C.: Clinical Studies on Venous Pressure. 1. Technique: Venous Pressure in Normal Individuals. Cuore e Circ. **29:** 97, 1945.

The authors studied the venous pressure of normal subjects by the direct method. A variation from usual technique was the graphic recording of the venous pressure. Oscillations of the venous pressure due to three possible causes were observed: (a) arterial pulsations (transmitted); (b) respiratory changes; (c) changes of the venous tonus.

The venous pressure tracings varied in different individuals and at times presented ample and frequent oscillations, caused by variations of venous tonus. Values between 20 and 170 mm. water were considered normal by the authors.

LUISADA.

Mallen, M. S., and Pallares, D. S.: A Study of Chronic Cor Pulmonale. Arch. Inst. cardiol. México **16:** 22, 1946.

Fourteen cases of chronic cor pulmonale were studied from both a clinical and electrocardiographic standpoint. The main symptoms and signs were paroxysmal dyspnea, effort dyspnea, cyanosis, and venous engorgement. Congestive failure was revealed by hepatic enlargement, edema, tachycardia, and prolongation of the arm-to-tongue time. Accentuation of the hilar shadows was present in all cases; enlargement of the pulmonary artery was observed in over 90 per cent of the patients.

The electrocardiographic changes were: P_2 higher than P_1; P wave inverted in V_1 but upright in V_F; absence of Q_1; presence of S_1 and Q_3; small R wave in V_3, V_4, V_5, V_6; deep S wave in V_4 and V_5; T inverted, flat or diphasic in Leads II, III, V_F, V_1, V_2, and V_3.

The above changes were attributed to dilatation and hypertrophy of the right auricle and ventricle.

LUISADA.

Elkin, D. C., and Banner, E. A.: Arteriovenous Aneurysm Following Surgical Operations. J. A. M. A. **131:** 1117 (Aug. 3), 1946.

This case was reported because of its rarity. The authors have not encountered a similar instance in the literature. Most of the cases of arteriovenous fistula which have been presented in the literature have arisen as a result of war wounds or from injuries incurred in civilian life. In this report, the authors described a case in which this lesion was produced during a surgical operation, hysterectomy. The most likely explanation of this occurrence is that in transfixing and ligating blood vessels the needle used for this purpose injured the artery and vein at the same time, with the subsequent production of a communication between them.

Following the removal of the arteriovenous fistula, the patient made an uneventful recovery.

BELLET.

Dock, W.: The Predilection of Atherosclerosis for the Coronary Arteries. J. A. M. A. **131:** 875 (July 13), 1946.

In this article, Dock makes two points: (1) that arteriosclerotic changes frequently occur earlier in the coronary vessels than in other vessels and (2) that coronary artery disease is more frequent in men than in women, especially before the seventh decade.

From a study of hundreds of soldiers who died of coronary disease, it was apparent that cases of coronary disease without tibial, cerebral, or aortic lesions, which are exceptional after the sixth decade, are the rule in men under 40 years. Coronary thrombosis is not only much more frequent, but also often occurs as a result of a purely local atheromatosis. In those hearts examined at necropsy it was noted that while most of the vessels were relatively free of atheroma, many of them had unusually thick intimal layers at places in the coronaries where no lipoid had yet been deposited and where there was no inflammatory reaction.

Although Spalteholz, Gross, and others mention the remarkable thickness of the coronary intima, as compared with that of the radial, tibial, cerebral, or visceral arteries, this observation has been ignored by most pathologists and clinicians. No satisfactory explanation of the increased susceptibility of the coronary arteries to atheroma has been thus far advanced.

Dock was unable to explain the higher incidence of coronary disease in men as compared with women from the level of the blood cholesterol or the height of the arterial pressure. In the examination of hearts of young adults killed in accidents, Dock observed a striking difference in the thickness of the coronary arteries in the two sexes. The men had thicker intimas; coronary arteries of boys no more than 18 years of age often had atheromas in them. In addition, sections were made of the right coronary artery, the left circumflex branch, and left descending branch of twelve infants of each sex who died less than twenty-four hours after birth. He observed in these specimens that the thickness of the coronary intima in male infants was about three times that in female infants.

He believes, therefore, that the sex differences in coronary disease and, to some extent, the familial differences in incidence seem to rest on an anatomic basis.

BELLET.

Hinton, J. W., and Lord, Jr., J. W.: Analysis of Surgical Failures and Fatalities Following Thoracolumbar Sympathectomy for Essential Hypertension. N. Y. State J. Med. **46:** 1714 (Aug.), 1946.

Although thoracolumbar sympathectomy has a definite place in the treatment of essential hypertension, there is no test or series of tests by which we can measure the chance for a successful result. In order to justify such a procedure, the surgeon must offer a much greater life expectancy

than that anticipated from the medical treatment of hypertension. After the various cardiac and renal function tests have been made, one can usually arrive at an opinion as to whether the patient is a safe surgical risk, but the final outcome following operation is difficult to prognosticate.

Patients in whom the pressure drops the most under sodium amytal seem to offer the highest percentage of good results. With reference to the question of age at the time of operation, the experience of these authors is as follows: in thirty-four cases including both sexes above 50 years of age at the time of operation, they found in six-month to three-year follow-ups that twenty-six, or 76.5 per cent, were improved, only eight, or 23.5 per cent, were unimproved, and that there were no deaths. This compares most favorably with the over-all failure and mortality figure for 152 cases, which was 20.5 per cent.

During the past four years, 227 patients have been operated upon for essential hypertension by these authors. One hundred fifty-two cases were operated upon by the Smithwick technic with follow-ups ranging from six months to three years. The total mortality of this group in and out of the hospital was 18, or 11.8 per cent. There have been thirteen patients, or 8.5 per cent, unimproved. This gives a total of poor results and fatalities of 20.5 per cent to date.

Since June, 1945, these authors have extended the operation to the higher thoracic ganglia and have included the ganglia from the third thoracic to the second lumbar inclusive. The immediate mortality was higher in the more extensive operative procedure. However, the authors hope the follow-ups will show better end results with a lower late or out-of-hospital mortality.

They grade the severity of the disease in the four major organs involved in essential hypertension, the eyes, cerebral vessels, heart, and kidneys, from 1 to 4 plus. If the degree of involvement in all organs exceeds 8 plus, they believe it is questionable whether a thoracolumbar sympathectomy will give any lasting results.

BELLET.

Griffith, J. Q., Jr., Padis, N., and Anthony, E.: Selection of Patients With Arterial Hypertension for Treatment by Repeated Injections of Pitressin. Am. J. M. Sc. **212:** 31 (July), 1946.

Sixty-three persons with hypertension were selected on the basis of (1) positive bio-assay for antidiuretic hormone in serum; (2) negative bio-assay for gonadotropic hormone in serum at the level of 330 mouse units; (3) normal renal function. It has been previously shown that cases of this type frequently respond to pituitary irradiation with a disappearance of the antidiuretic hormone and definite clinical improvement, the blood pressure often returning to the normal range. In view of the experience of Robinson and Farr with repeated injections of pitressin, it was considered probable that this might produce a result similar to that obtained with irradiation. Various methods of applying this treatment were tried; the one that appeared best was the administration of 1 c.c. of pitressin tannate in oil weekly for three weeks, then monthly for three months, and thereafter continuing the injections at monthly intervals until the bio-assay for antidiuretic hormone became and remained negative. Considering the group as a whole, the blood pressure was significantly lowered and symptoms improved in about one-half the cases.

When the procedure described was used, no reactions except a mild urticaria were observed; severe reactions did occur when aqueous pitressin was employed.

DURANT.

Levine, E. B., and Sellers, A. L.: Testosterone in Angina Pectoris. Am. J. M. Sc. **212:** 7 (July), 1946.

Testosterone propionate injected intramuscularly and methyl testosterone administered sublingually were found to have no value in the treatment of angina pectoris. However, testosterone preparations were found to be of definite value in relieving the chest discomfort sometimes associated with the male climacterium or the similar precordial ache of neurocirculatory asthenia occasionally encountered in individuals in the age group commonly subject to angina pectoris. In their field of usefulness, parenteral administration of 25 mg. of testosterone propionate two

to three times weekly was found to be preferable to the rather ineffective administration of methyl testosterone sublingually in doses of 10 to 15 mg. daily.

DURANT.

Griffith, G. C., Phillips, A. W., and Asher, C.: Pneumonitis Occurring in Rheumatic Fever. Am. J. M. Sc. **212:** 22 (July), 1946.

In a group of 1,046 rheumatic fever patients in a United States Naval Hospital, pneumonitis was found in 119 cases. A study of these cases revealed that pneumonitis is one of the prominent manifestations of active rheumatic fever. It is defined as a manifestation of rheumatic fever characterized by an inflammatory process of the lung and pleura, with an insidious onset, migrating consolidation, and frequent pleurisy with or without effusion. Occurring in approximately 11 per cent of rheumatic fever cases, it is seen in 53.1 per cent of the acute fulminating type, in 27.4 per cent of the polycyclic type, and in 2 per cent of the mild monocyclic type. Depending upon its time of appearance in the rheumatic fever state, three types may be recognized: primary acute, secondary acute, and subclinical. The diagnosis is based entirely on the exclusion of the other types of pneumonia and the concomitant development of other manifestations of acute rheumatic fever. The roentgen ray findings are not specific, but the rapid shift of the areas of density, the rapid development of an effusion, and the close adherence of the density to the bronchovascular markings are helpful findings. Laboratory aids are of little help in establishing the diagnosis. The importance of pneumonitis of rheumatic fever origin as one of the serious manifestations of rheumatic fever activity cannot be overemphasized.

DURANT.

Servelle, M.: Collateral Channels in Venous Obliteration. Arch. d. mal. du coeur. **39:** 2 (Jan.-Feb.), 1946.

The author states that there are few diseases of which knowledge is so limited as in the various forms of phlebitis. In reviewing his experiences with obliterative phlebitis of the extremities, he emphasizes the value of venography. This procedure, he points out, establishes a diagnosis which otherwise would be unrecognized until the appearance, years later, of varices, edema, and ulceration.

After obliteration of a large venous trunk, the circulation may be re-established by collateral channels developed from the branches of the main trunk or by recanalization. Obliterative phlebitis occurs in the femoral veins in 58 per cent of cases, in the popliteal veins in 22 per cent, in the iliac veins in 18 per cent, and in the calf veins in 8 per cent. Venography has demonstrated that primary varicosities are exceptional; varicosities are much more often secondary to venous obstruction. This fact explains the danger involved in sclerosing injections and surgical ablations which are performed blindly. What is commonly called the varicose ulcer is actually, in 80 per cent of cases, a postphlebitic ulcer.

LAPLACE.

Moses, W. R.: Ligation of the Inferior Vena Cava or Iliac Veins. A Report of 136 Operations. New England J. Med. **235:** 2 (July 4), 1946.

The clinical differentiation between thrombophlebitis which seldom causes embolism and phlebothrombosis which commonly causes embolism is often extremely difficult. Various tests proposed for this purpose are very unreliable, as is phlebography, the popularity of which has declined considerably.

In the prevention of embolism from peripheral phlebothrombosis, surgery has many advantages over anticoagulant therapy. The latter may cause serious hemorrhage, especially from a pulmonary infarct or in pregnancy. Second, anticoagulants probably do not affect the clots already formed but simply prevent their propagation. Third, the time when anticoagulants may be discontinued is uncertain. Finally, an anticoagulant usually entails more expense and loss of time to the patient.

The indications adopted for ligation of the inferior vena cava are thrombophlebitis of the pelvic veins with pulmonary embolism; pulmonary embolus associated with prostatic tenderness of re cent origin; pulmonary infarcts of obscure source; and venous occlusion in the lower extremities which would otherwise be treated by interruption of the femoral vein alone. Ligation of the vena cava is a more effective procedure than ligatior of the femoral veins of which it is a comple ment rather than a substitute. Ligation of the vena cava has an advantage over iliac ligation in preventing embolism not only from the affected limb, but also from an unrecognized source in the opposite apparently normal limb.

The operation involves an extraperitoneal approach, may be completed in ten to fifteen minutes, and is attended by a minimum of postoperative discomfort and complications. Collateral venous return is much more adequate than one would suppose, and edema of the legs is less than that which follows ligation of the femoral vein. In the author's experience, edema following vena cava ligation has invariably been accompanied by evidence of pre-existence or recurrence of the disease process. The author reports thirty-five cases: twenty-one ligations of the inferior vena cava and fifteen of the iliac vein. (These figures include one case in which both veins were ligated.) Under present tentative indications, caval ligation would have been preferable in the fifteen cases of iliac ligation. Twenty-two patients survived and thirteen died.

LAPLACE.

Kempner, W.: Some Effects of the Rice Diet Treatment of Kidney Disease and Hypertension. Bull. N. Y. Acad. Med. **22:** 358 (July), 1946.

The results of the use of the rice diet in 100 patients with primary kidney disease and in 222 patients with hypertensive vascular diseases are described. The diet is used in an attempt to reduce the amount of work required by the kidney cells, and thus reduce their demand for oxygen, in the presence of a pathologic condition which reduces the supply of oxygen.

The rice-fruit-sugar diet contains 2,000 calories, of which about 5 Gm. are fat and 20 Gm. are protein with not more than 0.2 Gm. of chloride and 0.15 Gm. of sodium. In seventy-nine patients with hypertensive cardiovascular disease, there was an average decrease in serum cholesterol of 57.3 milligrams.

In 203 of 322 patients in whom the rice diet was tried, there was objective improvement. Of the 100 patients with primary kidney disease, 65 per cent were improved. Of the 222 patients with hypertensive vascular disease, 62 per cent were improved. The author feels that dietary treatment should be tried before resorting to sympathectomy since the rice diet, if it proves to be ineffective, can simply be discontinued.

In 100 hypertensive patients studied electrocardiographically, there was a return to upright T waves in eleven of thirty-one patients with previously inverted T waves. In seventy-seven of eighty-seven patients the heart became smaller in size. In ten of the eighty-seven patients the heart became larger. Forty-four patients who had papilledema, hemorrhages, or exudates followed the rice diet for two months or longer. In all of them the retinopathy was arrested. In twenty of the forty-four patients, papilledema, hemorrhages, or exudates cleared up partially, and in twenty, completely.

NAIDE.

Piotti, A.: Paroxysmal Nodal Tachycardia in an Infant. Cardiologia **9:** 121, 3: 1945.

The author reports the clinical and pathologic findings in an 11-month-old child observed over a period of ten months. He had three attacks of nodal tachycardia, lasting twenty-three days, forty-six days, and seven months. During the attacks, the heart was markedly enlarged, the rate ranged from 160 to 280 per minute, the blood pressure was 80/60, and anorexia, weakness, pallor, cyanosis, massive edema, and heptomegaly were present. Between attacks the heart failure subsided spontaneously. The electrocardiogram taken during an attack showed negative P waves immediately preceding the QRS complexes. Between attacks the P waves were widened and notched. X-ray films showed tremendous enlargement of the left ventricle. There was a temporary response to ocular pressure, but no response to quinidine or gynergen was observed.

Digilanid was given throughout the course of treatment. The child had several bouts of rhinopharyngitis, one three months before onset of the tachycardia and others during his stay in the hospital. Death resulted from cardiac failure.

Autopsy revealed an interstitial myocarditis (Fiedler) located exclusively in the right auricle in the region where the connecting fibers from the coronary sinus (Kung's Brueckenfasern) join the Aschoff-Tawara node. The node itself was not involved. The entire conduction system was free from involvement. Serial sections through the entire heart failed to show other foci of myocarditis. There was severe dilatation and hypertrophy of all chambers. The nasopharyngitis was considered the possible etiologic factor of the myocarditis. The importance of serial sections is pointed out, as only part of the myocardium may be involved. The pathogenesis of the paroxysmal tachycardia is thought to be an alteration in the close and intimate contact between muscle fibers and nerve endings.

LENEL.

Chapuis, Jequier-Doze, and Werner: Newer Investigations on the Electrocardiogram in the Hypoxemic State. Helvet. med. acta. **19:** 519, 1945.

Comparisons were made between postexercise and posthypoxemia electrocardiograms in patients suspected of having coronary artery disease. The authors conclude that changes indicative of coronary insufficiency will appear following inhalation of gas mixtures with low oxygen tension, whereas such changes will be lacking in the electrocardiogram following effort. In their experience, chest lead CR_4 proved to be the best derivation for demonstrating the characteristic changes. Alterations resulting from sympathetic overactivity provoked by the hypoxemic states could be abolished by intravenous injection of DHE (dihydroergotamine). The authors suggest, therefore, that this drug offers a simple means for improving the accuracy of the "hypoxemia test" in differentiating changes due to structural cardiac disease from those due to reflex augmentations of adrenergic activity.

WENDKOS.

Thompson, L. E., and Gerstl, B.: Thromboangiitis of Pulmonary Vessels Associated With Aneurysm of Pulmonary Artery: Report of a Case. Arch. Int. Med. **77:** 614 (June), 1946.

This paper reports a case in which an aneurysm of the right pulmonary artery of more than 10 cm. in diameter developed within a period of three months and was associated with thromboangiitis of both pulmonary arteries and veins. The underlying cause of the changes in the pulmonary vessels was uncertain. *Streptococcus viridans* infection, syphilis, and congenital malformation were apparently excluded by the clinical course and by the laboratory and necropsy observations. The possibility was suggested that the lesions represented a variety of periarteritis nodosa, but this diagnosis could not be made with certainty.

BELLET.

Westerman, A.: On Calcifying, Scarifying Inflammations of the Pericardial Sac, and the Results of Operative Management. Arch. f. klin Chir. **205:** 549 (May 18), 1944.

Fifty-three patients with chronic constrictive and/or adhesive pericarditis who had total pericardiectomies by Schmieden and medical management by Volhard at the Frankfurt Clinic are reported. There were thirty-seven males and sixteen females; the majority were in the second to fourth decades of life at the time of operation. One-third of thirty-four patients operated on before 1939 made complete recoveries; one quarter showed definite improvement. Since 1939, slightly better results were observed: 64.2 per cent recovered or showed definite improvement.

Though the immediate operative mortality remains high, it is believed that total pericardiectomy gives much better results than the precordial cardiolysis of Brauer, although the mortality of the latter procedure is much lower at the operating table and even for a year postoperatively. Most autopsied cases showed a mixture of the constrictive and adhesive forms of chronic

pericarditis with little or no evidence of active infection. Aschoff bodies were never found and cultures were always negative, though occasionally histologic tuberculosis was present. The general impression was of a burnt-out process whose etiology was usually only suggested by the past medical history. This included some acute infection (rheumatic fever, sore throat, grippe, otitis, or pneumonia) in 68 per cent and tuberculosis in 9.4 per cent. In 19 per cent of the cases there was no clue as to the etiology.

The various types of acute and chronic pericarditis are described. The clinical picture and pathologic physiology of the adhesive variety (accretio cordis) with the systolic rib retraction and diastolic heart recoil (Brauer's sign) is distinguished from the constrictive variety (concretio cordis) with its interference with diastole and resultant venous congestion. However, this differentiation is clear cut more often clinically than pathologically. Both forms affect the function of the auricles and the right ventricle before the left ventricle, presumably because of the latter's thicker walls and higher pressure.

The importance of early operation while the heart muscle retains enough adaptability to function without its calcific encasement is stressed, as is pre- and postoperative medical care. The clinical diagnosis was often difficult.

The literature on experimental production of chronic pericarditis and the various forms of operative interference is reviewed. Pertinent data concerning each of the fifty-three cases are tabulated, with particular emphasis on the results of the operative procedure.

SAYEN.

McCutchen, G. T.: Varicosities of the Lower Extremity. Am. J. Surg. **72:** 63 (July), 1946.

Several methods of examining patients with varicose veins are re-emphasized. The author also describes a method for locating incompetent communicating veins or "perforators" as an operation on the venous system progresses. Patency of the deep venous circulation is determined by application of a tourniquet at the upper thigh for the great saphenous vein and just below the knee for the lesser saphenous. The tourniquet is applied with the patient in the upright position so that the veins are distended at the beginning of the test. The patient is allowed to walk a few steps. If the veins become less tense, the deep circulation is patent.

The method of locating incompetent communicating veins during an operation consists in placing the patient in the reverse Trendelenburg position (legs and trunk down) and advancing a tourniquet from below upward on the leg. At the points where perforators are suspected, the vein is exposed and severed between clamps. The perforator, if it is found, is treated in the same manner. Preliminary testing may be carried out by the application of two tourniquets at short distances from each other while the Trendelenburg position is assumed, followed by assumption of the reverse Trendelenburg position. However, it is believed that the ligation as described acts in a more effective manner than the lower tourniquet in stopping confusing flow from the distal points of the vein. A number of illustrations accompany the description of this method.

The extreme reverse Trendelenburg position should be assumed and maintained for five to ten minutes after all ligations are completed. If dilatation of any of the veins becomes manifest it may be assumed that an incompetent perforator has been overlooked and further search is in order.

NAIDE.

Cosgrove, Jr., C. E., and Kaump, D. H.: Endocardial Sclerosis in Infants and Children. Am J. Clin. Path. **16:** 322 (May), 1946.

The authors review the theories of the pathogenesis of endocardial sclerosis in infants and children and describe the pathologic findings listed by other observers. These findings are also compared with the findings in six cases of their own. Compositely these varied grossly from simple thickening and opacity of the endocardium to severely distorted valves in extreme instances. The myocardial changes seemed to parallel the extent of the endocardial involvement. The heart generally was enlarged due to myocardial fibrosis, myocardial hypertrophy, and dilatation of the ventricles. The coronary arteries were normal.

Microscopically the endocardial thickening was composed chiefly of collagenous connective tissue with some increase in elastic tissue, which in many areas extended as fingerlike projections between the myocardial fibers. Occasionally the thickening was nodular and resembled myxomatous tissue or possessed a cartilaginous-like component at the base of the valves. Occasional vessels in the endocardium showed much narrowing due to endothelial fibrosis. The myocardium frequently was markedly vascular and showed numerous areas of degeneration, varying from loss of muscle striation to necrosis. In none of the six cases was there definite indication of inflammatory changes as evidenced by myocardial giant cells or infiltration with lymphocytes or polymorphonuclear cells. The myocardial changes were particularly prominent in the papillary muscles and less frequent in the ventricular septum. Except for the Thebesian vessels, the veins of the myocardium were generally normal and no thromboses were found. When myocardial lesions occurred, they resembled infarctions rather than inflammatory lesions. This, together with the relative or complete occlusion of the smaller mural arterial and venous channels, inclined the authors to accept the probability that primary endocardial sclerosis is congenital. This impression was strengthened by the absence of evidences of inflammatory cell infiltration, the marked edema, the relatively young connective tissue, the lack of advancing proliferation of connective tissue, and the minimal tendency toward vascularization. Because of the high proportion of recorded illness in the mothers of these infants, the authors suggest that such illnesses of the mother during pregnancy, particularly early pregnancy, may be a factor in the production of endocardial sclerosis.

They conclude that the gross and microscopic characteristics of the lesions indicate that endocardial sclerosis in infants is a form of congenital heart disease.

MERANZE.

Estes, J. E., and Keith, N.: Hypothyroidism and Mild Myxedema from Thiocyanate Intoxication. Am. J. Med. **1**: 45 (July), 1946.

Thiocyanate therapy in a 62-year-old woman with hypertension caused definite symptoms of hypothyroidism and mild myxedema. Cardiac enlargement, demonstrated by roentgenographic examination, regressed upon withdrawal of the drug. During thiocyanate intoxication the electrocardiogram displayed an abnormally low total voltage of the QRS complexes and inverted, diphasic, and isoelectric T waves in various leads. The QRS complexes reverted to normal total voltage and the T waves became upright and of normal amplitude in all leads upon recovery from the intoxication.

The ultimate effects of hypothyroidism upon the heart are discussed. The cardiac enlargement seen in the teleoroentgenogram is generalized, involves all four chambers, and is currently viewed as a dilatation rather than a hypertrophy or pericardial effusion. The electrocardiographic changes are attributed to a reduction in cardiac conductivity rather than to reduction in skin conductivity.

FRIEDLAND.

Stewart, H. J., Evans, W. F., Brown, H. and Gerjuoy, J. R.: Peripheral Blood Flow, Rectal and Skin Temperature in Congestive Heart Failure: The Effects of Rapid Digitalization in This State. Arch. Int. Med. **77**: 643 (June), 1946.

It has been observed by various investigators that the temperature of the surface of cardiac patients is lower than in normal individuals, while that of patients with infectious fever is higher than normal. Certain experimental data point to a decrease in the amount of blood allotted to the peripheral blood flow in congestive heart failure.

Peripheral blood flow was measured in fifteen patients exhibiting congestive heart failure before and after administration of strophanthin K and digitaline Nativelle intravenously. Measurements of rectal and of skin temperature were recorded. Electrocardiograms, circulation time, and venous pressure were made to correlate with the measurements of the peripheral blood flow.

It was observed that the amount of blood flow allotted for the whole periphery of the body is within the normal range during heart failure as compared with the amount in normal subjects at

the same environmental temperature. Even though the same amount of blood is allotted to the peripheral circulation in heart failure, it is insufficient because of its slowed velocity in a vascular tree that is dilated to maintain an adequate elimination of heat in the face of the metabolic demands, so that the internal temperature of the body (rectal temperature) rises.

After the administration of strophanthin K intravenously, the peripheral blood flow increases. With the allocation of more blood to the periphery, the temperature of the skin rises and the body can now lose more heat by way of the skin, and its internal temperature (rectal temperature) falls slightly but does not usually reach normal levels over the intervals studied by the author.

BELLET.

Radner, S.: An Attempt at the Roentgenologic Visualization of Coronary Blood Vessels in Man. Acta. radiol. **26:** 497 (No. 6), 1945.

Using a modified technique of sternal puncture, a needle was inserted into the anterior upper mediastinum and then, under fluoroscopic guidance, into the ascending aorta. Twenty to 30 c.c. of thorotrast solution were injected rapidly. Five patients were studied by the technique. Of films taken in three cases, only one proved satisfactory. This film is reproduced and shows the aortic valves, the dye in the sinuses of Valsalva, and vague shadows of what appear to be the first portions of the coronary arteries. One patient developed mediastinal emphysema, and in one the needle penetrated the posterior aortic wall so that thorotrast was deposited in the pericardium, setting up a purulent inflammation which only very gradually resolved. At present, the problem of a satisfactory contrast medium has not been adequately solved.

SAŸEN.

Landis, E. M., Brown, E., Fauteaux, M., and Wise, C.: Central Venous Pressure in Relation to Cardiac "Competence," Blood Volume, and Exercise. J. Clin. Investigation **25:** 237 (March), 1946.

Evidence was obtained in anesthetized dogs to support the "back pressure" hypothesis of congestive heart failure. The dogs were exercised by electrical stimulation of all four limbs once each second. During control exercise, while cardiac function was normal, venous (right auricular) pressure, after a transient rise, fell to 96 mm. of water. After ligation of coronary arteries, resting venous pressure did not rise, but exercise was accompanied either by a decline in venous pressure, which was always less pronounced than that observed during control exercise, or by a definite rise. Electrically induced auricular fibrillation caused only slight rises in venous pressure, whereas combined auricular fibrillation plus exercise elevated venous pressure to higher levels. On the contrary, elevated resting venous pressure due to cardiac tamponade was lowered by exercise as in the control experiments, unless prior myocardial damage had reduced cardiac competence. Moreover, when venous pressure had been increased to extremely high levels by infusions of citrated whole blood or of Ringer's solution amounting to 50 per cent or more of the calculated blood volume, exercise was still capable of reducing the venous pressure.

A final set of experiments showed that during asphyxia, agonal arterial constriction effected a redistribution of approximately 20 per cent of the total circulating blood volume from the arterial to the venous bed. After auricular fibrillation and prolonged exercise, the blood redistributed to the venous bed during asphyxia amounted to about one-half the usual quantity, indicating that filtration had occurred during the high venous pressure incident to the combination of auricular fibrillation and exercise.

These experimental data provide the fundamentals for the development of a hypothesis of chronic congestive failure based upon the "back pressure" concept. Patients with reduced cardiac competence develop increased venous pressure during muscular activity. Effective circulating blood volume diminishes consequent to both sequestration of blood in the venous system and excessive filtration. Compensatory vasoconstriction occurs and is accompanied by reduced renal excretion of sodium and water and overproduction of erythrocytes and plasma proteins. Repeated muscular activity leads to secondary plethora or hypervolemia and eventuates in the typically high resting venous pressure of chronic congestive failure.

FRIEDLAND.

Book Reviews

LE TUMEURS ET LES POLYPES DU COEUR—ETUDE ANATOMO-CLINIQUE: By Dr. Ivan Mahaim.

Monographie de l'Institut d'Anatomie pathologique de l'Université de Lausanne. F. Roth et Cie, Editeurs, Lausanne; Masson et Cie, Editeurs, Paris, 1945. With 568 pages and 67 illustrations.

This book includes an exhaustive description and extensive discussion, with a fairly complete bibliography, of cases of primary and secondary tumors of the heart and pericardium. The author draws attention to the more frequent occurrence of these tumors than has been recognized hitherto by most clinicians or even many pathologists. He gives in detail the clinical signs and symptoms that should lead to a premortem diagnosis of these tumors, expecially in certain locations, and emphasizes the importance of considering this diagnosis in all cases of otherwise unexplained cardiac insufficiency. Much attention is paid in this book to the subject of polypoid growths, especially those within the left atrium or auricle, some of which are not truly neoplastic.

The benign polyps are the subject of extensive description and discussion, because the author believes that they may kill by obstructing the flow of blood from atrium to ventricle, either by valvular occlusion, or by atrial obliteration, and that a cure might be effected by surgical removal of these growths. In his opinion these tumors offer a challenge to the surgery of the future, and he even gives in detail the possible techniques that have occurred to him. The possibility of successful excision of some types of tumor of the pericardium is also considered.

The occurrence of embolism associated with intracardiac growths, especially of the polypoid type, is emphasized, and the author draws attention to the importance of embolectomy in cases of peripheral embolism. Such emboli are accessible to biopsy or removal, and histologic examination of the embolus can prove to be a great aid in the diagnosis of intracardiac tumors. In his experience, myxomatous tissue in a peripheral embolus in the systemic circulation means, almost unquestionably, the existence of a polyp in the left atrium or auricle; thrombotic tissue may mean a thrombotic polyp or myxomatous polyp covered with thrombus at the tip, or a mural thrombus in the left atrium, or, much less likely, in the left ventricle. He gives in full detail the clinical signs of an obstructive mass in the left atrium but states that there are no certain signs of an occlusive polyp in the right atrium. Particular emphasis is placed on the importance of basic simple clinical observations, and the inadequacy of some of the special and more expensive methods of investigation, for the purpose of the clinical diagnosis of tumors of heart and pericardium.

The book is well written and covers very thoroughly the description and discussion of all the known benign and malignant tumors of both heart and pericardium. It is an important and timely contribution to this subject and certainly constitutes a challenge to those who are interested in heroic surgery. It is his hope that, while surgeons are learning techniques for the possible excision of many of these tumors, physicians will busy themselves with learning how to make an early clinical diagnosis of what he considers an important cause of cardiac insufficiency.

HARRY GOLDBLATT.

American Heart Association, Inc.

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For the Study of the Circulation

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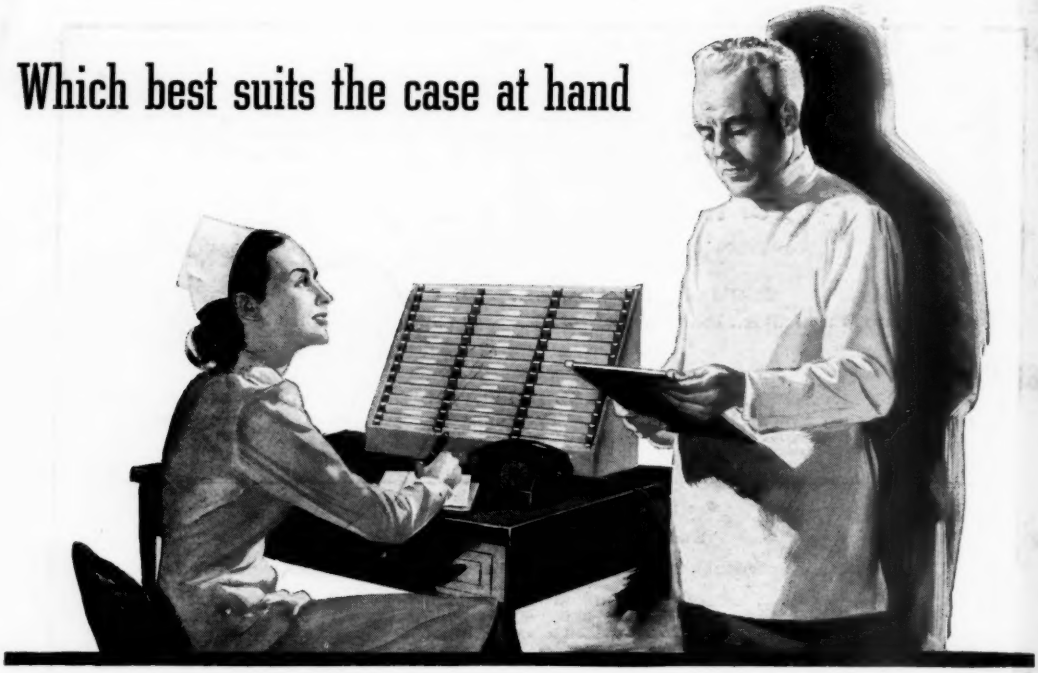
Which best suits the case at hand



ALTHOUGH most of the barbiturates do have the same general effects, there is a wide variation in their duration of action. This difference is particularly important because it enables the physician to choose the product which best suits the case at hand. For a short-acting barbiturate having a high therapeutic index and a relatively wide margin of safety, 'Seconal Sodium' (Sodium Propyl-methyl-carbinyl Allyl Barbiturate, Lilly) is often the choice. 'Seconal Sodium' has definite use in insomnia, nervousness, extreme fatigue with restlessness, and similar conditions.

In obstetrics, too, 'Seconal Sodium' is often preferred to the longer-acting barbiturates. 'Seconal Sodium' is supplied in 3/4-grain and 1 1/2-grain pulvules. Available on prescription at leading drug stores and in all hospital pharmacies.

Lilly

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